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# Nutritional strategies to optimize dairy cattle immunity[1]

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## ABSTRACT

Dairy cattle are susceptible to increased incidence and severity of both metabolic and infectious diseases during the periparturient period. A major contributing factor to increased health disorders is alterations in bovine immune mechanisms. Indeed, uncontrolled inflammation is a major contributing factor and a common link among several economically important infectious and metabolic diseases including mastitis, retained placenta, metritis, displaced abomasum, and ketosis. The nutritional status of dairy cows and the metabolism of specific nutrients are critical regulators of immune cell function. There is now a greater appreciation that certain mediators of the immune system can have a reciprocal effect on the metabolism of nutrients. Thus, any disturbances in nutritional or immunological homeostasis can provide deleterious feedback loops that can further enhance health disorders, increase production losses, and decrease the availability of safe and nutritious dairy foods for a growing global population. This review will discuss the complex interactions between nutrient metabolism and immune functions in periparturient dairy cattle. Details of how either deficiencies or overexposure to macro- and micronutrients can contribute to immune dysfunction and the subsequent development of health disorders will be presented. Specifically, the ways in which altered nutrient metabolism and oxidative stress can interact to compromise the immune system in transition cows will be discussed. A better understanding of the linkages between nutrition and immunity may facilitate the design of nutritional regimens that will reduce disease susceptibility in early lactation cows.

**Key words:** dairy cow, immunity, inflammation, metabolic stress

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## INTRODUCTION

Diseases of food animals represent a major deterrent to a profitable and sustainable animal agriculture sector. Dairy cattle in particular are susceptible to increased incidence and severity of both metabolic and infectious diseases during the periparturient period. Health problems occurring around the time of parturition are especially problematic because they greatly affect the productive efficiency of cows in the ensuing lactation. Direct economic losses associated with periparturient health disorders include reductions in the cow's productive capacity and increased mortality rates. Indirect economic losses associated with dairy cattle diseases include the costs of antimicrobial drugs, vaccines, and surveillance measures, and the labor needed to implement treatment and control measures (Pritchett et al., 2005). The ability of dairy cattle to resist the establishment of diseases during the periparturient period is related, in part, to the efficiency of their immune system. The immune system consists of a variety of biological components and processes that serve to protect animals from the consequences of disease. The primary roles of the immune system are to prevent microbial invasion of the body, eliminate existing infections and other sources of cellular injury, and restore tissues to normal function. In dairy cattle, the immune system utilizes a multifaceted network of physical, cellular, and soluble factors to facilitate defense against a diverse array of microbial challenges (Mallard et al., 1998; Rainard and Riollet, 2006; Aitken et al., 2011). This integrated system of defense mechanisms is highly regulated to maintain a delicate balance between the activation of immunity needed to prevent establishment of disease and the resolution of activity once the threat of invasion has passed. This paper will provide a brief overview of the bovine immune system, describe how suboptimal immune responses can fail to prevent disease, describe the interrelationship between nutrition and immune functions, and outline current strategies to optimize immune responses in dairy cows during times of increased susceptibility to disease. Given the critical role that nutrition plays in supporting all immune functions, nutritional-based management strategies should have a central position in any disease prevention program.

## IMMUNE SYSTEM OVERVIEW

A properly functioning immune system should protect dairy cows from a variety of pathogenic organisms, including viruses, bacteria, and parasites. To accomplish this task, the immune system utilizes a complex and dynamic network of tissues, cells, and molecules that can be conveniently separated into 2 distinct categories: innate immunity and adaptive or acquired immunity. The innate immune system is characterized by an early and rapid response that can occur within seconds following the initial tissue insult. Innate immunity is broad in scope with the capacity to respond to any tissue injury or neutralize a wide variety of potential pathogens. The adaptive immune system is delayed compared with innate immunity and can take several days to mount a response. Adaptive immunity is a more customized or specific response to infectious pathogens and can be augmented by repeated exposure to the same microbe. Collectively, the innate and adaptive immune systems must work synergistically to provide optimal protection from external threats and survival of the cow. Previous reviews provided detailed descriptions of the bovine immune system within the context of the periparturient cows (Mallard et al., 1998; Sordillo and Streicher, 2002; Aitken et al., 2011). Therefore, this review will provide only a brief overview of the major components of dairy cattle immunity with more emphasis on how nutritional status and specific nutrients affect essential aspects of host defense.

### *Innate Immune System*

The innate immune system is the dominant host defense mechanism in most organisms. Innate immunity includes the nonspecific components of the immune system that can respond to infectious microbes in a generic manner. Constituents of innate immunity represent the first line of defense against invading pathogens because they are already present or are activated quickly at the site of pathogen exposure. Depending on the efficiency of innate defenses, microbes may be eliminated within minutes to hours following invasion. This initial line of defense can be so rapid and efficient that there may be no noticeable changes in normal physiological functions of tissues as a consequence of the attempted microbial invasion. Because of its nonspecific nature, however, the innate immune mechanism is not augmented by repeated exposure to the same insult. Major components of the innate immune system include physical and mechanical barriers, phagocytes, vascular endothelium, and various soluble mediators derived from both immune and nonimmune cell populations within affected tissues (Table 1). Physical and mechanical barriers are essential for preventing pathogens from entering the body. Some examples of surface barrier defenses that impede microbial invasion include the skin, tears, and mucus. Once pathogens are able to breach this initial line of defense, however, the cellular and soluble components of the innate immune response must act promptly to prevent the successful establishment of disease.

Pattern recognition receptors (**PRR**) play a critical role in innate immunity by sensing the presence of invading pathogens that successfully breach surface barrier defenses. These PRR function to recognize a range of microbial factors associated with infectious pathogens and can be expressed on cell surfaces, secreted, or expressed intracellularly (Jungi et al., 2011; Kumar et al., 2011). The first PRR identified was Toll in *Drosophila melanogaster*, and the toll-like receptors (**TLR**) are now among the most widely studied PRR in mammals (Kawai and Akira, 2011). At least 10 different bovine TLR have been identified and can bind a range of microbial products and endogenous ligands collectively referred to as pathogen-associated molecular patterns (**PAMP**; McGuire et al., 2006). Some examples of PAMP that are unique to specific groups of

**Table 1**. Components of the innate immune system

| Factor | Main functions |
|---|---|
| Physical barriers | Block and trap microbes (skin, tears, mucus) |
| Pattern recognition receptors | Surveillance and activation of innate immune responses |
| Complement | Bacteriolytic and facilitates phagocytosis |
| Cytokines | Immunoregulatory for innate and adaptive immunity |
| Oxylipids | Proinflammatory and proresolving |
| Endothelial cells | Regulates leukocyte migration and activation |
| Neutrophils | Phagocytosis; antibacterial enzymes, defensins, and reactive oxygen species; neutrophil extracellular trap (NET) formation |
| Macrophages | Phagocytosis; production of cytokines and oxylipids |
| Dendritic cells | Phagocytosis; links innate and adaptive immunity |
| Natural killer cells | Targets and helps to eliminate infected host cells |