Dairy cows are particularly susceptible to infections of the mammary gland for several weeks around the time of parturition in part due to an incompetent immune system. Neutrophils are a primary component of the innate immune response. Efficient migration of these neutrophils into the mammary gland and subsequent antimicrobial activity are crucial for the resolution of the intramammary infection. Three experiments were conducted to investigate the mechanisms of neutrophil dysfunction during the periparturient period and test potential nutritional strategies to prevent the immune-alteration. In the first experiment, Escherichia coli lipopolysaccharide, a component of the bacterial cell wall, stimulated the function of bovine neutrophils and gene expression of selected genes encoding for cytokines and enzymes involved in the production of antimicrobial compounds. In the second experiment, a B-vitamin dietary and yeast supplement down-regulated the expression of genes that enriched the lysosome pathway and decreased the expression of transcripts in the oxidative phosphorylation pathway. In the third study, cows supplemented with trace minerals from inorganic sources had a slight increase in phagocytosis, compared with cows receiving no supplemental trace minerals. Furthermore, organic trace mineral supplementation (vs. inorganic) up-regulated gene pathways involved in antigen recognition and immune response. Improving our understanding of periparturient immunobiology and the roots of immunosuppression will facilitate the development of interventions to reduce the incidence and severity of clinical mastitis in dairy cows. In addition, nutritional strategies such as dietary supplementation with micronutrients may boost the host immune response and enhance resistance against intramammary infections.