Immune Surveillance of Mammary Tissue by Phagocytic Cells

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Abstract: The leukocytes in milk consist of lymphocytes, neutrophil polymorphonuclear leukocytes (PMN) and macrophages. Lymphocytes together with antigen-presenting cells function in the generation of an effective immune response. Lymphocytes can be divided into two distinct subsets, T- and B- lymphocytes, that differ in function and protein products. The professional phagocytic cells of the bovine mammary gland are PMN and macrophages. In the normal mammary gland macrophages are the predominate cells which act as sentinels to invading mastitis causing pathogens. Once the invaders are detected, macrophages release chemical messengers called chemoattractants that cause the directed migration of PMN into the infection. Migration of neutrophils into mammary tissue provides the first immunological line of defense against bacteria that penetrate the physical barrier of the teat canal. However, their presence is like a double-edged sword. While the PMN are phagocytosing and destroying the invading pathogens, they inadvertently release chemicals which induces swelling of secretory epithelium cytoplasm, sloughing of secretory cells, and decreased secretory activity. Permanent scarring will result in a loss of milk production. Resident and newly migrated macrophages help reduce the damage to the epithelium by phagocytosing PMN that undergo programmed cell death through a process called apoptosis. Specific ligands on the neutrophil surface are required for directed migration and phagocytosis. In response to infection, freshly migrated leukocytes express greater numbers of cell surface receptors for immunoglobulins complement and are more phagocytic than their counterparts in blood. However, phagocytic activity rapidly decreases with continued exposure to inhibitory factors such as milk fat globules and casein in mammary secretions. Compensatory hypertrophy in
non-mastitic quarters partially compensates for lost milk production in diseased quarters. Advances in molecular biology are making available the tools, techniques, and products to study and modulate host-parasite interactions. For example the cloning and expression of proteins that bind endotoxin may provide ways of reducing damaging effects of endotoxin during acute coliform mastitis. The successful formation of bifunctional monoclonal antibodies for the targeted lysis of mastitis causing bacteria represents a new line of therapeutics for the control of mastitis in dairy cows.

1. INTRODUCTION

The first line of defense against mammary infection is the teat canal. Bacteria that pass this barrier and enter the teat cistern meet the second line of defense: phagocytic leukocytes. Phagocytes, consisting of neutrophil polymorphonuclear leukocytes (PMN) and macrophages, ingest and kill mastitis pathogens. Bacterial invasion and growth within the mammary gland is the main cause of mastitis. Invading bacteria settle next to the epithelial cells lining the mammary ducts, absorbing nutrients from milk while expelling harmful toxins that attack and destroy the epithelium. While helpless against the invading horde of bacteria, the epithelium and white blood cells called macrophages soon release chemical messengers called cytokines that signal the body for help. These chemicals increase blood flow to the udder and open spaces between the endothelial cells lining the capillary bed of the udder allowing for the release of blood plasma into the milk. If this bacterium has been encountered before, specific antibodies will pass into the milk along with the plasma. Soon PMN, a specialized form of white blood cells, migrate directly from blood into the bacterial hoard. The PMN release potent oxidants that destroy not only some of the bacteria but also some of the epithelial cells lining the ducts and alveoli within the udder. The PMN also combats the bacteria directly by ingestion or phagocytosis, aided by antibodies that attach to the bacteria and allow the PMN to recognize them as foreign. For the PMN it is a dead end mission. After ingestion and release of their chemicals most of the PMN perish. Next macrophages migrate in through the pores of the capillaries. Damage to the epithelium is limited by induction of programmed cell death (apoptosis) in PMN and their engulfment by macrophages. Through this process damaging chemicals are walled off within dying PMN that are then ingested by macrophages to minimize damage to the epithelium of the udder. Within several hours lymphocytes arrive at the site of the infection and take the battle to another level of immunological defense, as they recognize antigens through membrane receptors that are specific for invading pathogens. Soon