

# Michigan Dairy Review

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## Bovine Leukosis Virus Update II: Impact on Immunity and Disease Resistance

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*Bovine Leukosis Virus (BLV) causes leukemia and alters the normal immune defenses of cattle. This article describes how the virus infects cattle and the potential impact BLV may have on susceptibility to other infectious diseases.*

### Introduction

Bovine Leukosis Virus (BLV) is a retroviral infection that causes leukemia in cattle by targeting white blood cells and causing them to grow uncontrollably. Most BLV-infected cattle seldom present with outward clinical signs. Approximately 30% of infected animals, however, will have abnormally high white blood cell counts and up to 5% will develop malignant tumors or lymphosarcomas. The most severe cases of BLV will exhibit enlarged lymph nodes, weight loss, loss of appetite, infertility and decreased milk production [1, 2]. The virus is transferred from cow to cow by BLV-laden white blood cells found in blood, saliva, semen and milk.

Certain management practices that expose uninfected animals to contaminated blood, such as the use of common needles, contaminated surgical instruments and multiuse rectal sleeves, can dramatically increase the prevalence of BLV within a herd. There is also evidence to suggest that BLV-infected dams may transmit the virus to offspring via colostrum or placental transfer.

Once infected with BLV, cattle become lifetime carriers since there are no vaccines or treatments that can eliminate the infection. Indeed, a recent survey of the US dairy cattle farms suggest that over 80% of all dairy farms have cows that have BLV infection ([http://nahms.aphis.usda.gov/dairy/dairy07/Dairy2007\\_BLV.pdf](http://nahms.aphis.usda.gov/dairy/dairy07/Dairy2007_BLV.pdf)). Economic losses associated with BLV and management practices that can reduce or eliminate transmission of BLV from infected carriers to future replacement animals was covered in a previous article (<https://www.msu.edu/user/mdr/vol14no1/erskine.html>). This article will focus on how the virus attacks important host defense mechanisms and the potential impact on susceptibility to other infectious diseases.

### Bovine Immunity and BLV Pathogenesis

Cattle are protected by a variety of immune defense mechanisms, which can be separated into two distinct categories: innate immunity and acquired immunity. Innate immunity, also known as nonspecific responsiveness, includes a set of resistance mechanisms that are not

specific to a particular pathogen. Innate immunity is present or activated quickly at the site of infection by numerous stimuli; however, they are not augmented by repeated exposure to the same insult.

Conversely, the specific or acquired immune system recognizes specific pathogen (antigens) that activate selective elimination of that pathogen. Recognition of antigens is mediated by antibody molecules, cytokines, and a specialized group of white blood cells (lymphocytes). Lymphocytes are the only cells of the immune system that recognize antigens through membrane receptors that are specific for invading pathogens. There are two distinct subsets of lymphocytes, which differ in function and protein products, T and B lymphocytes. Because of the “memory” of certain lymphocytes, acquired immune responses can be augmented by repeated exposure to a particular pathogen [3].

Vaccination of cattle against certain pathogens can occur if acquired immune mechanisms are effectively activated. Whereas it is convenient to discuss the highly complex nature of the bovine immune system in terms of nonspecific and specific responses, it should be emphasized that innate and acquired immunity does not operate independent of each other. Deficiencies in any one aspect of the immune response could greatly impact the ability of cattle to resist infectious diseases.

The primary cellular targets of BLV infection are B-lymphocytes. Once infected, B-lymphocyte populations increase significantly due to abnormal growth resulting in a persistent lymphocytosis and eventually malignant lymphomas. The primary roles of B-lymphocytes are to help recognize invading pathogens and then produce specific antibodies needed to eliminate the pathogen. BLV infection impairs B-lymphocyte functions, especially in persistently lymphocytotic animals. The progression of BLV also is known to affect other aspects of host defense.

As B-lymphocyte numbers increase in BLV-infected cattle, there are significant decreases in the percentages of the T-lymphocytes [4]. T-lymphocytes are needed to recognize pathogens and then secrete a repertoire of soluble factors (cytokines) that regulate essentially all aspects of innate and acquired immunity. The development of bovine leukemia is clearly a complex process involving altered regulation of both the numbers and function of bovine immune cell populations. Therefore, essential components of the acquired immune response are impaired in BLV-infected cattle.

### Effects of BLV on Health and Productivity

The appearance of lymphomas in BLV-infected dairy cows has a direct economic impact on the industry due to increased replacement costs, loss of income from condemned carcasses of cull cows, and the inability to export cattle, semen and embryos to countries that maintain BLV control programs. Other losses may include reduced reproductive efficiency and decreased milk production [1, 2].

The impact of BLV infection on herd health and economy may be more extensive, however, because of the pronounced effect of BLV on the immune system. Indeed, the dramatic shift in the distribution and functional capabilities of bovine lymphocyte populations was suggested to have a detrimental impact on the ability of cattle to resist the development of other infectious diseases [5]. For example, an epidemiologist reported a significant association between BLV infection and the occurrence of both clinical and subclinical mastitis [2, 6, 7]. BLV-infected herds also were found to have a higher risk of hoof problems, gastroenteritis,

pneumonia, and culling when compared with BLV-free herds [7]. Whereas these observational studies do not necessarily prove that BLV causes these other health disorders, the potential impact on the ability of cows to resist the development of other health disorders is worth a closer examination.

One area of investigation that has received very little attention is the potential impact of BLV status and altered immune function on vaccine efficacy. Vaccine trials have been performed in attempts to vaccinate against BLV with some promising results [8-10]. However, there are limited published reports on how cows may respond to non-BLV related immunization protocols based on BLV status. Unfortunately, the impact of BLV status on other vaccine programs has not been investigated.

The possibility that BLV infection may alter the efficacy of vaccine programs and decrease host resistance to other diseases is an intriguing hypothesis. The J5 *Escherichia coli* bacterin is extensively used in cattle to enhance immune resistance against gram-negative bacteria, including mastitis-causing coliforms. Studies are underway at MSU to determine if altered immune status in BLV infected dairy cattle may influence the effectiveness of J5 vaccination protocols. Our initial results confirm that lymphocyte homeostasis is disrupted in BLV-infected cattle and changes in immune cell functions are related to the severity and duration of lymphocytosis.

The dramatic shifts in both T- and B-lymphocyte populations were accompanied by significant changes in the expression of cytokines that are involved in enhancing the immune response during vaccination. We are now evaluating antibody responses to the J5 bacterin with respect to BLV status. If these initial studies suggest a link between BLV status and responsiveness to vaccine protocols, larger field studies will be designed to examine in more detail how BLV infection may impact herd vaccine programs.

The implications of this research on the health and disease resistance in dairy cattle reach beyond increasing our knowledge of the effects of BLV on the bovine immune system. The prevailing belief is that BLV is not a major health issue in most herds as only a small group (<5%) succumb to lymphosarcoma. However, if we determine that that BLV infection alters the ability of the bovine immune system to respond to immunization, the implications for maintaining the health and wellbeing of dairy cattle in the face of infectious challenge from mastitis pathogens, and potentially other infectious diseases, could provide more economic incentive to implement management practices that would minimize the risk of spread within the herd.

### **Acknowledgements**

The authors wish to acknowledge the Elwood Kirkpatrick Dairy Science fund for the generous research support.

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