

Reference Point

Options for the control of bovine leukemia virus in dairy cattle

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The subclinical impact of bovine leukemia virus (BLV) on the sustainability of the US dairy industry is only now being fully recognized. Findings of recent longitudinal studies conducted in Michigan dairy herds were consistent with the results of previous studies in showing that within-herd prevalence of BLV-infected cattle was negatively associated with milk production and cow longevity. Risk factors relating to routes of hematogenous transmission such as the use of shared hypodermic needles, shared reproductive examination sleeves, and natural breeding were associated with BLV within-herd prevalence. Few US dairy producers know the prevalence of BLV-infected cattle in their herds or are aware of the insidious economic impact of BLV or the options for BLV control. As an increasing number of countries eradicate BLV from their cattle populations, restrictions on the movement of US cattle and cattle products will likely increase. Veterinarians should be aware of recent developments for screening serum and milk samples for antibodies against BLV and the results of research regarding the economic impact of BLV so they can advise their dairy clients of available alternatives for monitoring and controlling BLV infection. (*J Am Vet Med Assoc* 2014;244:914–922)

Enzootic bovine leukosis is a contagious retroviral disease of cattle caused by BLV. Nearly 40% of BLV-infected cattle will develop persistent lymphocytosis within a few years of infection (Figure 1)¹; however, < 5% of infected cattle develop malignant lymphosarcoma, the most common neoplastic disease identified in cattle slaughtered in the United States.^{1–3} In the 1960s and 1970s, BLV prevalence rates in cattle in the United States and Canada were approximately 10%, and the only recognized impact of infection was BLV-induced lymphosarcoma.^{3–7} Consequently, the US and Canadian cattle industries decided that BLV was not sufficiently problematic to warrant control. In contrast, 21 countries and Western Australia have now successfully eradicated BLV from their cattle herds.^{8,9} However, in the United States, approximately 40% of dairy cattle are now infected with BLV, and costs associated with subclinical BLV infection have now become apparent.^{4,10–12} Results of multiple studies^{13–16} indicate that BLV infection degrades lymphocyte function in cattle, which diminishes the immune response to vaccinations and opportunistic infections. Investigators of multiple studies^{4,10–12} report that BLV infection impairs milk production and cow longevity. Additionally, export of US dairy cattle and cattle products may become increasingly difficult as more

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ABBREVIATIONS

BLV	Bovine leukemia virus
BoLA	Bovine leukocyte antigen
DHI	Dairy herd improvement
SCC	Somatic cell count

countries attempt to maintain their BLV-free status or implement BLV eradication programs.¹⁷

For these reasons, US dairy producers need to make informed decisions about whether BLV control is feasible for their operations. Because BLV is a retrovirus, prospects for an effective vaccine are problematic. Genetic selection for BLV-resistant cattle might be beneficial for minimizing economic losses, but it currently appears that complete resistance to BLV cannot be obtained by selection of cattle with BLV-resistant alleles of the DRB3.2 gene that has been the subject of recent research.^{18,19} Hence, the US cattle industry may need to use management interventions to reduce BLV prevalence to a sufficiently low level so that test-and-segregate and test-and-removal control programs become economically feasible. In a recent longitudinal study^{4,10} conducted by our field epidemiology group, 15 of 113 Michigan dairy herds had no evidence of cattle with antibodies against BLV, which suggests that BLV-negative herds can be maintained, even in a state where most dairy herds contain BLV-infected cattle. Traditionally, management practices recommended for the control of BLV transmission have included single use of hypodermic needles and reproductive examination sleeves, use of artificial insemination instead of bulls for breeding purposes, control of stable flies and other biting insects, segregation

of infected cattle, feeding calves only heat-treated colostrum or colostrum replacers, and cleaning and disinfecting blood-contaminated equipment between animals during routine procedures such as application of ear tags, tattooing, and dehorning.^{5,11,17} Accurate estimates of the cost-effectiveness of BLV control measures are required, as are methods to identify and overcome educational, behavioral, and attitudinal barriers to the additional expenditures, labor, and inconvenience necessary for the control of BLV. Because the importance of different routes of BLV transmission will likely vary by farm, each dairy farm may need a customized BLV control program and have to routinely monitor its BLV prevalence to determine the program's effectiveness.

Implementation of ELISA screening of milk samples for anti-BLV antibodies to detect cows subclinically infected with BLV is somewhat analogous to the adoption of individual-cow SCC to screen cows for subclinical mastitis in previous decades. When the capability to determine individual-cow SCC first became available to US dairy operations, producers did not realize the economic impact of subclinical mastitis or know how to interpret the SCC data. Consequently, they rarely requested individual-cow SCC testing from their DHI organizations. Wide-scale usage of SCC data was greatly augmented by educational and extension programs to teach dairy producers about the economic impact of subclinical mastitis and ways that SCC data can be used as an effective monitoring tool. Although an ELISA to test milk from individual cows for antibodies against BLV (ie, BLV milk ELISA) is now available to US dairy herds through their DHI testing service, only approximately 0.5% of US dairy cows are tested for BLV annually.⁴ Many producers do not yet appreciate the costs incurred to their operations because of subclinical BLV infection or know how to use diagnostic test results to monitor BLV transmission within their herds.¹¹ The BLV milk ELISA has been proposed as a science-based tool that can be used by dairy producers

to monitor within-herd BLV prevalence, and may become used more frequently as was the individual-cow SCC. Herd veterinarians can help producers use new BLV-screening technologies to reduce BLV in their herds and perhaps eventually qualify for BLV-free certification. Currently, the United States does not have a national eradication program for BLV, but individual dairy producers can qualify for state and privately certified BLV-free programs.^{20–24}

BLV Prevalence and Economic Losses

According to USDA surveys,^{6,7} 39% and 83% of US beef cow-calf and dairy herds, respectively, contain BLV-infected cattle. The within-herd BLV prevalence ranges from 23% to 46% in affected dairy herds.^{5,25,26} Malignant lymphosarcoma induced by BLV is the largest single reason that US cattle are condemned during postmortem inspection at slaughter plants. Surveys^{3,27} indicate that malignant lymphosarcoma accounts for 13.5% of beef cattle condemnations and 26.9% of dairy cattle condemnations at US slaughter plants. Annual economic losses to the US dairy industry associated with BLV are estimated to be \$285 million for producers and \$240 million for consumers; however, the subclinical impact of BLV infection on cow longevity is not included in those estimates.^{5,19}

Milk Production

The USDA National Animal Health Monitoring System 1996 dairy study⁵ determined that 95 kg of milk/cow/y was lost for each 10% increase in the within-herd BLV prevalence, and investigators of a more recent Michigan study⁴ reported similar herd-level production losses associated with BLV. The association between within-herd BLV prevalence and milk production per cow per year for both the USDA⁵ and Michigan⁴ studies was summarized (Figure 2).²⁸ Accurate determination of the effect of BLV

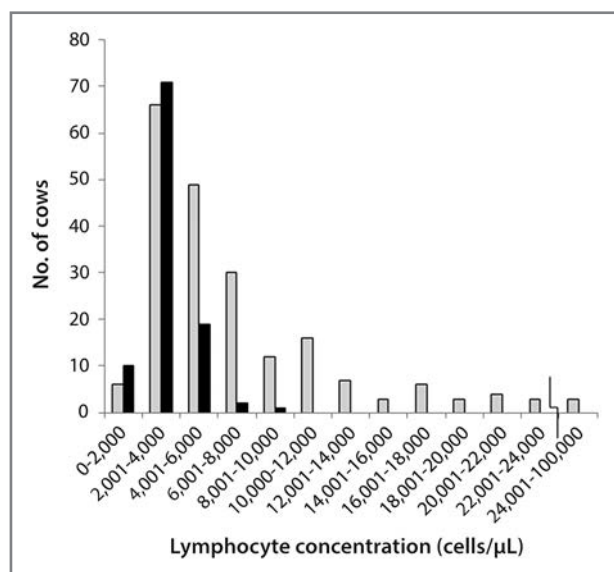


Figure 1—Absolute lymphocyte concentration for 208 BLV-positive (gray bars) and 103 BLV-negative (black bars) cows in 5 dairy herds in Michigan (n = 2), Wisconsin (1), Iowa (1), and Pennsylvania (1) during 2008 through 2010. (From Swenson CL, Erskine RJ, Bartlett PC. Impact of bovine leukemia virus infection on neutrophil and lymphocyte concentrations in dairy cattle. *J Am Vet Med Assoc* 2013;243:131–135. Reprinted with permission.)

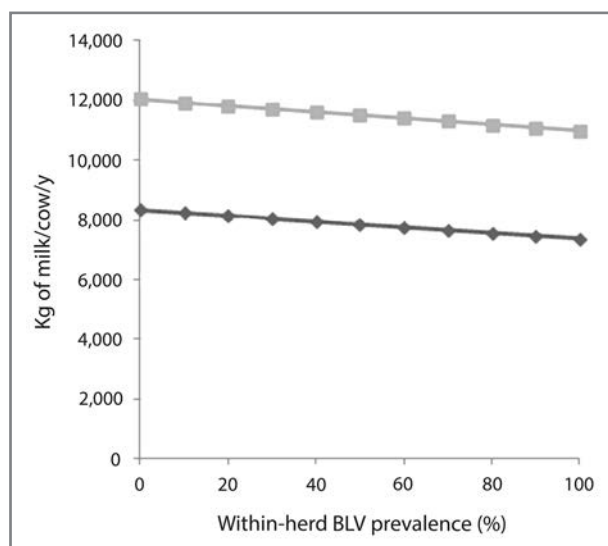


Figure 2—Association between within-herd BLV prevalence and milk production per cow per year for a study of 113 dairy herds in Michigan conducted in 2010 (gray squares) and the National Animal Health Monitoring System dairy study conducted in 1996 (black diamonds). (Adapted from Erskine RJ, Bartlett PC. Bovine leukemia virus: final summary of the 2010 Michigan study. *Michigan Dairy Review* 2012;17(3):1–4. Reprinted with permission.)

infection on milk production is confounded by lactation number and cow longevity. Compared with young cows, older cows tend to produce more milk and are also more likely to be infected with BLV (Figure 3).^{4,10,11,29} To further complicate the issue, results of a couple of studies^{10,29} suggest that BLV-infected cows produce as much or more milk than do their uninfected herdmates until the lactation during which their immune systems become substantially compromised, often resulting in culling before their 305-day mature equivalent milk production is severely affected. Investigators of another study³⁰ reported that BLV-infected cows with persistent lymphocytosis did not achieve their predicted genetic-value milk or fat production. Because BLV infection adversely affects cow longevity, dairy herds with a high BLV prevalence tend to have a low mean cow age because the older, BLV-infected cows are frequently culled.^{10,12} Consequently, estimation of the true impact of BLV infection on milk production is difficult, which is most likely why the effect of BLV on dairy productivity has been so long unrecognized and underappreciated. Preliminary analysis of the same database used for a recent survival analysis¹² involved a 2-level hierarchical model with lactation number and herd (random effect), and results indicate a significant negative association between BLV-infected cows and milk production, which is consistent with findings at the herd level.¹⁰

Cow Longevity

In a Michigan study,¹⁰ the proportion of older cows (lactation number, ≥ 3) decreased as the within-herd BLV prevalence increased. This suggested that BLV-infected cows might have decreased longevity, compared with that of their noninfected herdmates, and led to another study,¹² in which 3,849 dairy cows in 112 herds were followed for a mean of 597 days after being tested for antibodies against BLV with the BLV milk ELISA. Results of that study¹² indicate that cows with antibodies against BLV were significantly ($P < 0.001$) more likely to die or be culled (hazard ratio, 1.23) during the observation period

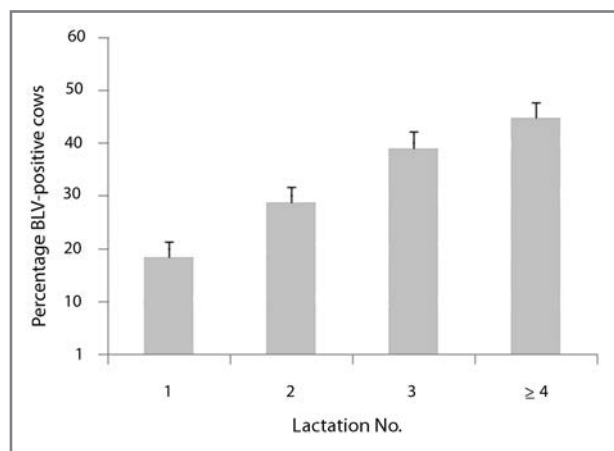


Figure 3—Mean prevalence (95% confidence limits) of BLV test-positive cows by lactation from 113 Michigan dairy herds. The BLV status of individual cows was determined by an ELISA for detection of antibodies against BLV in milk. (From Erskine RJ, Bartlett PC, Byrem TM, et al. Using a herd profile to determine age-specific prevalence of bovine leukemia virus in Michigan dairy herds. *J Vet Med Int* 2012;2012:350374. Reprinted with permission.)

than were herdmates that did not have antibodies against BLV. Further, the survival probability was significantly associated with BLV antibody titer in a dose-response manner. As milk BLV antibody titer increased, survival probability decreased; cows with the highest BLV antibody titers (BLV milk ELISA optical density results > 0.50) were at 40% greater risk of dying or being culled than were cows without antibodies against BLV (Figure 4).¹² A dose-response association is an important criterion for determination of a causal relationship, and this association warrants analysis at the national level. Controlling BLV may enhance the sustainability of the dairy industry by enabling cows to live longer and reach their full (ie, mature equivalent) milk production and economic potential.

Losses associated with subclinical BLV infection are difficult to quantify because the virus compromises immune function and is thought to increase the susceptibility of infected animals to multiple opportunistic pathogens, thereby collectively contributing to BLV's economic impact. Although results of multiple studies^{12,29,31-35} indicate that BLV infection impairs cow longevity, this finding is not corroborated by the findings of other studies.^{36,37} Tiwari et al³⁸ reported that BLV-infected cows tend to have reduced longevity, compared with uninfected cows; however, this association between BLV status and longevity was not statistically significant ($P < 0.30$) when herd and lactation number were controlled in the model. In a study³⁹ of dairy herds in Ontario, Canada, the cull rate for cattle seropositive for antibodies against BLV was 27% higher than the cull rate for cattle seronegative for antibodies against BLV, although that effect was only observed in older cows (lactation number ≥ 3). In that study³⁹ and the study¹² conducted in Michigan, the association between individual-cow BLV status and longevity was stronger for multiparous cows than for primiparous cows.

BLV Management Risk Factors

In a study¹¹ conducted by our group, the within-herd BLV prevalence for 113 Michigan dairy herds was

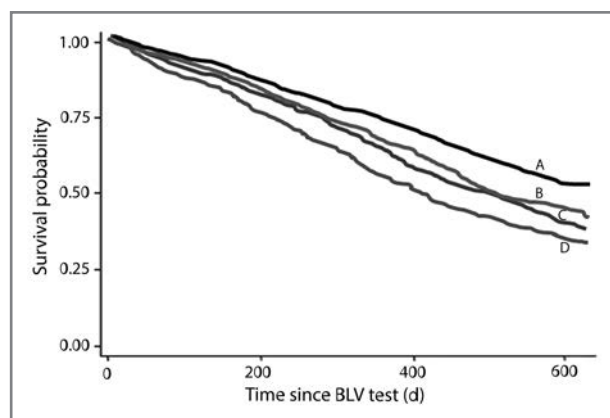


Figure 4—Survival probability of 3,849 cows from 112 Michigan dairy herds that were tested for antibodies against BLV by means of an ELISA performed on milk samples (BLV milk ELISA). Cows were classified into 1 of 4 categories on the basis of the BLV milk ELISA results (BLV negative, A [n = 2,536]; optical density ≥ 0.1 to 0.25, B [418]; optical density > 0.25 to 0.50, C [521]; optical density > 0.50 , D [374]). Herd and lactation number were controlled in the model. (Adapted from Bartlett PC, Norby B, Byrem TM, et al. Bovine leukemia virus and cow longevity in Michigan dairy herds. *J Dairy Sci* 2013;96:1591-1597. Reprinted with permission.)

determined by means of the BLV milk ELISA and the managers of those herds were interviewed regarding herd management practices to identify risk factors associated with increasing within-herd BLV prevalence. Results of a multivariable analysis¹¹ with a robust R^2 value of 0.43 identified several management practices positively associated with within-herd BLV prevalence. Those practices included reuse of unsterilized hypodermic needles, lack of fly control, gouge-type dehorning, increasing number of reproductive examinations (almost always performed without changing reproductive examination sleeves between cows), and increasing number of injections to adult cows during the nonlactating period immediately prior to parturition.¹¹ Additionally, exclusive use of artificial insemination to breed heifers was associated with a decreased BLV prevalence, compared with that associated with the use of natural service (ie, bulls) to breed heifers.¹¹ Although intervention studies are needed before causal relationships can be inferred, multivariable analysis helps to reduce confounding to reveal those factors that are independently associated with anti-BLV antibody prevalence, and therefore identify associations that are more likely to be causal in nature.

At the national level, control of BLV has involved programs that emphasize various combinations of 3 approaches (management interventions with ongoing monitoring, test and segregate, and test and slaughter).⁴⁰⁻⁴² In a study⁴² conducted in a dairy herd with a high within-herd BLV prevalence, implementation of single-use hypodermic needles and reproductive examination sleeves, disinfection of tattoo equipment, use of cautery-type dehorning, and feeding of milk replacer and heat-treated colostrum resulted in a decrease in the prevalence of BLV-infected heifers from 44% to 17% in 2 years without selective culling or segregation of BLV-infected cattle. Management practices associated with an increase in the risk of hematogenous BLV transmission identified in other studies⁴³⁻⁵⁰ include gouge-type dehorning and not changing hypodermic needles or disinfecting tattoo pliers between cattle. Prevention of hematogenous transmission of BLV may also prevent transmission of other pathogens such as *Anaplasma*.⁵¹ Failure to change examination sleeves between cows following artificial insemination or reproductive examination has also been identified as a risk factor for the hematogenous transmission of BLV.^{4,42} Internationally, segregation and culling of cows that test positive for antibodies against BLV are practices commonly used to control and eradicate BLV from cattle populations.^{41,47}

In humans, a frequent route of transmission for HIV (the retrovirus that causes AIDS) is the exchange of blood through rectal bleeding; therefore, it seems reasonable to hypothesize that this route may also be important for the transmission of other retroviruses such as BLV. In cows, frequently performed procedures such as rectal examination and artificial insemination involve the insertion of a sleeve-covered arm into the rectum, and it is not uncommon for rectal bleeding to be associated with these procedures. In the study¹¹ of Michigan dairy herds to identify risk factors associated with within-herd BLV prevalence, reproductive examination sleeves were routinely changed between

each cow on only 5 of 113 herds and occurred too infrequently to assess statistically. However, BLV was not detected in 2 of those 5 herds and the remaining 3 herds had a low within-herd BLV prevalence (mean, 5.8%), whereas the mean within-herd BLV prevalence for all 113 herds was 33%.¹¹ Results of that study¹¹ also indicate that the number of reproductive examinations per cow is positively associated ($P = 0.03$) with BLV prevalence. These findings suggest that the use of a clean reproductive examination sleeve for each cow during artificial insemination or rectal examination could minimize BLV transmission.

Another finding in the Michigan study¹¹ was that the use of natural service to breed heifers and cows was positively associated with BLV prevalence. Other studies^{45,52,53} have also identified natural service as a risk factor for BLV infection. During natural service, the exchange of blood resulting from penile or vaginal trauma is the most likely route of BLV transmission. The exclusive use of artificial insemination for breeding purposes might reduce BLV transmission in a herd. Another recommended practice is to use only bulls that test negative for antibodies against BLV in natural service breeding programs. In BLV-affected herds, this may require repeated testing of bulls on a routine basis.

Results of multiple studies^{11,50,54} indicate that lack of a fly-control program is a risk factor for BLV infection, which suggests that biting flies play an important role in BLV transmission. Cyromazine, a US-licensed fly-control product, has a reported efficacy of 97% against biting stable flies (*Stomoxys calcitrans*) and might be beneficial for reducing BLV transmission.^{49,50,54-59} Cyromazine targets biological systems that are only found in arthropods; therefore, its toxicity to vertebrates is very low, and its use obviates the need for the use of other insecticides, which are more dangerous to the environment and both animal and human health.⁵⁵

For each of 113 Michigan dairy herds, the BLV milk ELISA was used to detect antibodies against BLV in the milk of the 10 most recently calved cows in each of the first, second, third, and fourth and later lactations.^{4,10} The lactation-specific BLV prevalence was calculated as the proportion of tested cows within a given lactation that had antibodies against BLV in their milk, and the within-herd BLV prevalence was calculated as the mean of the 4 lactation-specific BLV prevalences.⁴ Of those 113 herds, 15 (13.3%) had no cows test positive for antibodies against BLV and 41 (36.3%) had no first-lactation cows test positive for antibodies against BLV.^{4,10} These findings show that it is possible to maintain BLV-free dairy herds in a state where most dairy herds contain BLV-infected cattle. Bovine leukemia virus has been eradicated from all cattle in 12 European countries since 2003 and from 8 additional European countries and New Zealand since 2011.^{8,9,60} Additionally, BLV has been eradicated from most regions of Poland, Portugal, and Italy. In Western Australia, BLV has been successfully eradicated from dairy herds but the government has decided to not attempt eradication of BLV from beef herds, which have a very low prevalence of infected cattle.⁶¹

Given the relatively high prevalence of BLV-infected cows in most US dairy herds, culling of all cows that test positive for antibodies against BLV would be prohibitively expensive.⁴¹ The implementation of management practices to reduce BLV transmission might eventually decrease the prevalence of BLV-infected cattle on dairy herds to a level sufficiently low so that test-and-segregate or test-and-slaughter programs would be feasible and the United States could follow the example of the many other countries that have eradicated BLV from their cattle populations. Many European countries, the states of New York and Missouri, and the US Animal Health Association offer BLV-free certification programs, and for a herd to become certified BLV-free, it generally has to have no cows test positive for BLV on 2 or more consecutive semiannual herd tests.^{20–24}

BLV Immunology

The most obvious immunologic effect of BLV infection is a peripheral blood lymphocytosis, which may be indicative of the start of altered immune function.¹ Bovine leukemia virus is lymphotropic and is believed to cause peripheral blood mononuclear cell proliferation and altered apoptosis and cytokine production.¹ Results of a preliminary study¹³ suggest that following vaccination, BLV-infected dairy cattle have an impaired humoral immune response, compared with that of noninfected dairy cattle. Infection with BLV induces accumulation of B lymphocytes in blood and lymphoid tissue^{62–64} with concurrent decreases in the percentages of CD4+ and CD8+ T lymphocytes.⁶⁴ The BLV provirus has been detected in the DNA of immunoaffinity-purified T lymphocytes from BLV-infected cattle.⁶⁵ Concentrations of certain type 1 cytokines, including interleukins 2 and 12 and interferon- γ , from CD4+ T lymphocytes are reduced from basal levels in BLV-infected cattle, and this altered cytokine production could be responsible for suppressed mitogen-induced T-lymphocyte proliferation.^{64,66,67} Additionally, BLV-infected T cells have increased expression of immunoinhibitory receptors, which in turn enhance the ability of pathogens that cause chronic infections to evade immune defenses (eg, by increasing expression of interleukin-10 and decreasing expression of interferon- γ).^{15,16} This expression of immunoinhibitory receptors is positively correlated with proviral load.¹⁶

Control Through Genetic Selection

Investigators of 1 study³⁵ reported that dairy cow longevity was associated with genetic resistance to persistent lymphocytosis. A major histocompatibility complex class I allele (BoLA-A) that is associated with susceptibility to persistent lymphocytosis is also associated with high milk production potential.³⁵ Wu et al³⁰ reported that BLV-infected cows with high genetic potentials for milk and fat yields were more susceptible to developing lymphocytosis than were cows with lower genetic milk and fat yield potentials, and lymphocytotic cows failed to achieve their predicted genetic potential milk and fat yields. Some authors have suggested that certain polymorphisms of BoLA-DRB3.2 are associated with high BLV proviral loads, and cattle with polymorphisms associated with low BLV proviral loads are relatively

noninfectious to their herdmates.^{18,19} It is possible that genetic selection could be used to breed cattle that are resistant to developing high BLV proviral loads¹⁸; however, in other reports,^{19,68} 40% (21/53) of BLV-infected cows with a high BLV proviral load were not lymphocytotic and 23% (27/119) of cows with the BoLA-DRB3.2 allele that is thought to confer resistance to BLV had a high BLV proviral load. Thus, genetic selection for BLV-resistant cattle may be more difficult than the simple selection of cattle with the DRB3.2 gene. Results of a study⁶⁹ of 114 Holstein herds and 8 Jersey herds indicate that the heritability of BLV infection was only 8% for both breeds. However, genetic factors may play an important role in determining the degree of immune system alteration if and when an animal is infected by the virus.

Public Perception Regarding Food Safety and Animal Welfare

The viability and sustainability of the dairy industry are extremely vulnerable to consumer perceptions of food safety and animal welfare. The human health implications of BLV have been extensively studied and debated. Historically, all available epidemiological evidence has indicated that BLV was not a human health hazard, but the issue may now be less clear. In BLV-infected cattle without lymphosarcoma, it was previously believed that the virus induced only a benign proliferation of polyclonal B lymphocytes, but findings of more recent immunologic studies^{13,14,70,71,b} suggest that some lymphocyte proliferation may indeed be malignant in those cattle. Moreover, evidence suggests that BLV will grow in tissue cultures of human cells,^{70,72,b} and most humans exposed to the virus will produce antibodies against it.^{70,73} Additionally, genes of BLV origin have been identified in human mammary cells, although results are conflicting regarding whether those genes are found more frequently in cancerous or noncancerous tissues.^{70,72,b} In North America, where BLV is prevalent in the cattle population, the rate of breast cancer in women remains lower than that in countries of Western Europe where BLV has long been eradicated from the cattle population.⁷⁴ Clearly, further research regarding the human health implications of BLV and other animal retroviruses is warranted.

Public concerns regarding the welfare of BLV-infected cattle could also damage the dairy industry's sustainability if consumers believe that infected cattle die slowly from immunosuppression induced by the virus. Bovine leukemia virus has been incorrectly referred to as cattle AIDS by detractors of food animal industries.⁷⁵ The ideal life for a food animal is one that is comfortable, healthy, and free of pain until they are humanely stunned and slaughtered so that their bodies can become food. The finding that survival probability of BLV-infected cows decreases as BLV antibody titer increases (Figure 4)¹² lends support to the theory that BLV-infected cattle may slowly debilitate with a multitude of opportunistic infections and production problems as a result of BLV-induced immunosuppression.

At some point, foreign and domestic consumers of US dairy products may prefer products produced by cattle uninfected with BLV, regardless of whether there is scientifically based evidence indicating that dairy

and beef products produced by BLV-infected cattle are as safe as those produced by uninfected cattle. Public perception might be exploited by industry antagonists to scare consumers and damage the sustainability of the US dairy industry in a global market where many other nations have made BLV control a priority.

BLV in Beef Cattle

Beef cattle infected with BLV may serve as a reservoir and source for virus transmission to dairy cattle by direct contact and hematogenously via biting flies and use of BLV-contaminated needles, tattoo pliers, or surgical equipment. Further, BLV-infected beef cattle may represent an obstacle to any regional eradication efforts to establish certified BLV-free regions within the United States. It is unknown whether the US beef industry will be motivated to control BLV. Estimates of within-herd BLV prevalence in US beef herds are few and range from 1.2% to 10.3%.^{76–79} Beef herds generally have a lower within-herd BLV prevalence than do dairy herds.^{5–7,25,26,77–80} In a recent survey^c of 6 beef feedlot operations and 6 dairy herds in Michigan, 48% of dairy cattle had serum antibodies against BLV, whereas only 10% of feedlot cattle were seropositive for antibodies against BLV. In another survey⁸¹ of 363 beef bulls owned by 124 producers in Michigan that was conducted during the spring of 2009 (n = 156 bulls) and 2013 (207 bulls), the crude prevalence of bulls with serum antibodies against BLV was 24.7%, with the age-specific BLV prevalence increasing from 1% in 1-year-old bulls to 67% in bulls \geq 5 years old (Figure 5). This finding suggests that most beef bulls do not become infected with BLV until after they start breeding cows. When considered in conjunction with the relatively low prevalence of BLV-infected beef cows, this suggests that natural service might have a more important role in BLV transmission than previously realized and is consistent with the reported association between natural service and increasing BLV prevalence in dairy herds.¹¹

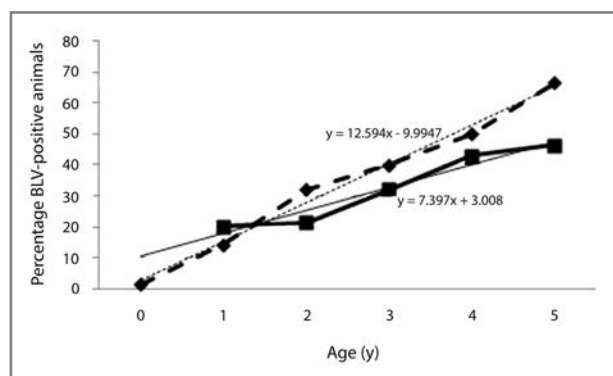


Figure 5—Percentage of beef bulls (diamonds) and dairy cows (squares) that tested positive for antibodies against BLV by age. The BLV test status of beef bulls (363 bulls from 124 Michigan beef herds) was determined by means of an ELISA performed on serum samples obtained during breeding soundness examinations in the spring of 2009 and 2012. The BLV test status of dairy cows (4,300 cows from 113 Michigan dairy herds) was determined by means of an ELISA performed on milk samples obtained after parturition during 2010. The regression line of best fit is provided for each group of cattle. (Adapted from Zalucha J, Grooms DL, Erskine RJ, et al. Bovine leukemia virus in Michigan beef bulls. *Clin Theriogenol* 2013;5:441–447. Reprinted with permission.)

BLV Control

The decision to implement a farm BLV control program requires a comparison of the costs incurred by the disease with the costs incurred to control the disease. Traditionally, the only recognized costs incurred by BLV infection were those associated with lymphosarcoma; however, on the basis of results of recent studies,^{10,12} it is now apparent that costs associated with lost milk production and decreased cow longevity also need to be considered. Also, as more countries maintain or attempt BLV eradication, the US dairy export market may diminish and be increasingly burdened with demands for preshipment BLV testing.

The BLV Herd Profile

Dairy producers who implement a BLV control program must have a method to monitor the progress of that program. The BLV herd profile is a standardized way of sampling 40 cattle in a herd that enables the calculation of lactation-specific prevalence rates and yet still provides a precise and accurate measure of overall herd prevalence.⁴ Herds participating in a DHI program ask their DHI technicians to request milk ELISA testing for BLV on the milk samples from the 10 cows that most recently calved in each of the first, second, third, and fourth and later lactations. It is crucial that this sampling procedure be followed without deviation; producers could bias the BLV prevalence estimates if they selectively choose to test cows that they suspect are or are not infected with the virus. For the BLV herd profile, the lactation-specific BLV prevalence is calculated as the proportion of tested cows with positive BLV milk ELISA results within a given lactation. The overall within-herd BLV prevalence is estimated as the mean of the 4 lactation-specific BLV prevalences. The within-herd BLV prevalence calculated for the BLV herd profile is almost perfectly correlated ($R^2 = 0.99$) with the actual within-herd prevalence obtained by testing all cattle in the herd.⁴

A significant positive association exists between age and the lactation-specific BLV prevalence (Figure 3).⁴ The BLV herd profile is essentially age adjusted in that it is independent of the age distribution of cows within the herd. It was designed to identify the age cohort with the highest percentage of BLV-infected cows and allow producers to compare the prevalence of BLV-infected cattle before and after cows enter the lactating herd. This information can be used to help identify areas of potential risk for BLV transmission so that control programs can be developed, assessed, and modified. For example, depending on the herd size, most of the milk samples tested from first-lactation cows are obtained within the first few weeks after parturition, and any of those cows with antibodies against BLV were likely infected prior to entering the lactating herd. If a high percentage of first-lactation cows have antibodies against BLV, the producer should focus control efforts on preventing virus transmission among calves and replacement heifers rather than in the lactating herd. In the Michigan study,⁴ 41 of 113 (36%) dairy herds had a first-lactation BLV prevalence of 0, and those herds should focus control efforts on preventing virus transmission within the milking

herd. One of the benefits of the BLV herd profile is that results can be fairly compared among herds with different age distributions or within the same herd over time regardless of changes in the age distribution.

Options for Control

The progression of BLV control options currently available to US dairy producers is summarized (Table 1). Some producers might choose to do nothing to minimize or prevent BLV transmission (option 1). For producers who are interested in implementing a BLV control program, the first step is to conduct a single BLV herd profile to determine the lactation-specific and within-herd BLV prevalence. If the within-herd BLV prevalence is 0, the producer might decide to pursue BLV-free herd certification. If the within-herd BLV prevalence is very low, implementation of management practices to minimize BLV transmission in conjunction with culling or segregation of BLV-infected cattle (option 3) should enable the producer to pursue BLV-free herd certification within a relatively short period of time. If the within-herd BLV prevalence is high, the most cost-effective approach for BLV control might be to implement comprehensive or select management practices to minimize BLV transmission and lower prevalence (option 2) before progressing to options 3 or 4.

Studies to determine the proportion of BLV infections attributable to each potential route of transmission are lacking. It is likely that the results of such studies will vary among herds. For example, most BLV infections in some herds might be attributable to gouge-type dehorning, whereas in other herds, most BLV infections might be attributed to reuse of BLV-contaminated hypodermic needles, the bites of stable flies, or some other hematogenous route of transmission. The extent to which each management practice minimizes or prevents BLV transmission on a particular farm is almost always unknown. Therefore, some producers may choose to implement a comprehensive program to prevent BLV transmission, whereas others may choose to implement only a few selected control practices and use an annual or semiannual BLV herd profile to assess the effectiveness of those practices. Generally, European countries used options 3 and 4 to achieve national BLV eradication; however, the prevalence of BLV in those countries was typically much lower than that in the United States.^{41,82} Further study is necessary to determine the effectiveness of specific management practices (Table 2) for preventing BLV transmission and reducing BLV prevalence.

Dairy producers who are unwilling or economically unable to implement a comprehensive BLV control program (ie, apply all management practices recommended for BLV control) might develop BLV control protocols on the basis of perceived costs and benefits. For example, producers might require veterinarians and artificial insemination technicians to change reproductive examination sleeves before reuse for the next cow only if blood is observed on the sleeve. Producers who continue to reuse hypodermic needles might inject BLV test-negative cattle with a different needle than they use for BLV test-positive cattle. Similarly, reproductive sleeves could be reused within groups of BLV test-negative and BLV test-positive cattle. Although there are

many methods for controlling various species of flies, it is likely BLV is mainly transmitted by biting stable flies and not by nuisance house flies; therefore, producers might select fly control strategies that specifically target stable flies. Finally, producers unable to use artificial insemination exclusively for breeding purposes might elect to use only bulls that test negative for BLV.

Additionally, some producers may choose to retest the serum or milk from the same cohort of cows that had negative BLV test results in a previous period. This approach will enable calculation of the incidence of new BLV infections. The incidence of new BLV infections may be a more dynamic measure of the efficacy of a BLV control program than is within-herd prevalence and may allow producers to adjust their control programs in a more timely and efficient manner than does the BLV herd profile. Comparison of new infection rates between the spring and fall should be a good indication of the importance of biting flies on BLV transmission.

At some point, producers with low within-herd BLV prevalences might choose to pursue BLV control options 3 or 4 (Table 1) to eradicate the disease from their herds. Once BLV is eradicated from a herd, the costs should be minimal for periodic testing to maintain a BLV-free status as prescribed by the certifying organization. In Great Britain, bulk tank milk samples are screened for antibodies against BLV as part of the national program to maintain its BLV-free status,⁸³ and a similar approach might be possible in the United States.

Table 1—Options for BLV control on US dairy operations.

1. No action.
2. Monitor BLV prevalence with BLV herd profile milk testing or traditional serum testing. Make comprehensive or selected management changes to reduce transmission and thereby reduce prevalence.
3. Test all cattle and segregate BLV test–positive cattle. Make selected management changes to reduce transmission. Maintain a closed herd or only add BLV test–negative cattle that retest negative after a quarantine period.
4. Test and cull BLV-positive cattle. Maintain a closed herd or only add BLV test–negative cattle that retest negative after a quarantine period.

Table 2—Suggested management practices to minimize BLV transmission within dairy herds.

1. Use a sterile hypodermic needle for each cow.
2. Clean and disinfect blood-contaminated equipment for dehorning, tattooing, supernumerary teat removal, and other surgical procedures between animals.
3. Use a new or cleaned and disinfected reproductive examination sleeve for each cow.
4. Use artificial insemination exclusively for breeding purposes.
5. Control stable and other biting flies.
6. Minimize contact between newborn calves and BLV-positive cattle.
7. Avoid feeding unpasteurized colostrum from BLV-positive cows to newborn calves. (Feed newborn calves heat-treated colostrum, banked colostrum from BLV-negative cows, or colostrum replacer.)
8. Segregate BLV test–positive cattle from BLV test–negative cattle.
9. Cull or segregate BLV-positive cattle with lymphocytosis.

Summary

Recent research has identified previously unappreciated costs associated with BLV infection. Dairy veterinarians need to be prepared to recommend and help implement BLV monitoring and control programs that are customized for each herd on the basis of its needs and limitations. The BLV milk ELISA, which is currently available through all DHI organizations, can be a valuable part of such BLV monitoring and control programs.

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