

Bovine Leukemia Virus (BLV) in Your Herd? Get rid of it!

Frank van der Meer and Alessa Kuczewski

University of Calgary, Faculty of Veterinary Medicine, Calgary, AB
Email: frank.vandermeer@ucalgary.ca

■ Take Home Messages

- Bovine leukosis, caused by bovine leukemia virus (BLV) has a significant negative impact on farm profitability.
- Controlling BLV is possible with relatively straightforward measures. These measures also have a positive influence on the control of other pathogens.
- Controlling or even eradicating BLV from the dairy herd will pay for itself through increased milk production and improved longevity.
- Bovine leukemia virus does not cause disease in humans; however, the general population can view the presence of a 'tumour causing virus' in the dairy population negatively.
- Bovine leukosis control needs to focus on colostrum management, single use of needles, use of clean palpation gloves, proper dehorning technique and the use of artificial insemination or BLV negative bulls.

■ Bovine Leukosis, What is the Cause?

Bovine leukosis is a disease, a tumour of the white blood cells, specifically in a subgroup of B-cells. These cells get infected with a virus called bovine leukemia virus (BLV). The most important characteristic of these types of viruses is that they make copies of themselves, which then integrate in the cow's genome. Therefore, once a cow gets infected with BLV, it can never get rid of this virus. The B-cells that get infected are a component of the immune system; they play an important role in the defence against infections and help the cow maintain its health. When infection with BLV occurs, these cells will change and will not function properly anymore; hence, the immune system of these animals will be suboptimal (Frie and Coussens, 2015). We can therefore expect that BLV-infected cows will have a higher chance of developing other diseases.

■ How Do I Know I Have BLV in My Herd?

When BLV infects a cow it can lead to different outcomes. Only a small fraction of the infected animals will develop tumours; this means that most of the infected animals will not easily be recognized. The circulation of BLV in the herd can stay under the radar for quite a long time.

To find out if BLV is present, laboratory testing is the only reliable option. There are several diagnostic tests marketed; they can be used on milk or blood to find out if the animals have produced antibodies. These antibodies are a sign that the immune system has recognized that BLV has infected the animal and has responded to that threat. As previously stated, this virus will now be in the host genome; the cow cannot get rid of it. This means that once antibodies can be detected in the cow she will be infected for life; you do not have to demonstrate that the virus is still present—it always will be. These antibody tests are very reliable and have low error rates; therefore, they are a good way to screen the herd. Testing is an important measure to understand what is going on in the herd and is an integral part of any control program.

As stated before, a very large proportion of dairy cows in North America is infected with BLV, so if cows are purchased without testing, the chance that BLV is introduced in the herd is very high. It is rare to find a herd that is still free of BLV; we estimate that >90% of all herds in Canada have at least one BLV-infected animal. BLV is also one of the most important causes of loss of revenue of live animal export. BLV antibody-positive animals will be blocked from transport to BLV-free nations (including many countries in Europe, New Zealand and Australia).

■ Will a BLV Positive Animal Always Die?

Generally, less than 5% of the BLV-infected animals will eventually develop tumours. Once the animal has tumours, it will die very quickly; there is no cure. The other 95% of the animals will not be as easy to recognize. A large group (up to 50%) of the infected animals will develop a persistent lymphocytosis, which means that a large proportion of the infected B-cells are abnormal, and the cow will suffer more often from other infections and diseases. These are also the animals that are likely to develop tumours later in life. These conditions will lead to decreased milk production and reduced longevity and will impact animal welfare.

Animals vary in the number of BLV virus copies that integrate in their genome. These integrated viruses are called proviruses. The more proviruses that are present in the cells, the higher the likelihood that the infected animal can transmit the virus to other animals, including to the calves through, for example, colostrum. This is an important group of animals because they pose

the highest risk for maintaining virus circulation in the herd. Unfortunately, we cannot recognize these 'high proviral load' animals with the previously mentioned antibody test; we need a more specific test to identify them. This test is called quantitative PCR, and although it is a more complicated test method, it might be an important tool for control in herds where a relatively high number of animals is infected.

The difficulty of recognizing infected animals, and the need for laboratory testing to confirm infection, can lead to infection of the herd being overlooked quite easily, with many animals becoming infected before the seriousness of the situation is understood.

■ **Can I Get Infected with BLV When I Drink Milk or Eat Meat from an Infected Cow?**

There is no proof that BLV can infect humans. It is very doubtful that BLV can infect a human cell because generally these viruses are very host specific. With pasteurization of milk, as is routinely done in many countries, and proper preparation of meat, the virus is easily inactivated. Recently, several scientific articles were published out of the USA suggesting that BLV causes breast cancer (Buehring et al., 2015). There are serious doubts about these studies and several other researchers have demonstrated that BLV cannot be found in human tumour tissue (Gillet and Willems, 2016).

Even though the virus can be easily inactivated we must still be proactive in controlling BLV. The public may become very disgruntled with the fact that in our dairy herds viruses are circulating that cause tumours in cows. Control of BLV will therefore not only contribute to animal welfare and the economic prosperity of the farm, but hopefully also to the trust the consumers have in the quality of milk and its production methods.

■ **Many Countries are Free of BLV; Why is it Still Here in North America?**

The simple answer to the question posed above is, we did not care and did not pay attention. When the prevalence was still low in dairy herds, nobody recognized the need to control this virus, especially because there was no proof that BLV caused significant economic damage. BLV was considered unimportant, and that gave the virus the opportunity to slowly, but surely, infect more animals and more herds. Changes in management, such as expansion of herds, increased use of injections, and other herd practices have facilitated BLV transmission.

Recently, researchers from Michigan State University demonstrated that infection with BLV can significantly reduce milk production and negatively

impact cow longevity (Bartlett et al., 2013). Many of the older studies (1980s-2000s) provide conflicting information, or the studies were done in situations that cannot be compared to the current North American production system and level of infection with BLV. In Europe the control of BLV started when there were still relatively few animals infected; therefore, the removal of positive animals was still possible. Also, this control program was (partially) financed by the governments. Because it is unlikely that the provincial or federal government will finance BLV control, and that ~40% of the animals in North American herds are infected, alternative strategies to remove this virus from our herds are needed. Realistically, voluntary control has always been a weak strategy, because compliance with control measures is sometimes difficult. But it is not impossible, and when many farmers can be convinced of the value of such a program, and a good, farm focused, strategy can be developed, we have a good chance of success.

■ BLV Control is it Financially Worth It?

The main question asked when BLV control is discussed is whether it is economically worthwhile. The investments in labour and equipment should be compensated with increased revenue. It is an important question that will determine the success of a control strategy.

Specifically, with the unique supply-managed system of Canada, economic evaluations that have been done for other economic systems such as a free market system in the US cannot be easily applied to Canada. Therefore, we decided to do an Alberta-specific evaluation, which has also more relevance for dairy producers in the other Canadian provinces. We compared four different control strategies: 1) All proposed management strategies that can be used to control BLV are implemented and the expected reduction of BLV prevalence in the herd is quick; 2) We implement some of the management strategies, leading to a slower reduction of BLV prevalence, but this is most likely a more realistic scenario on many farms; 3) We test animals for infection with BLV, and the positive animals are removed from the farm. This is a likely scenario when a farmer is very motivated to remove BLV from the farm or when the prevalence is relatively low; and 4) We place the animals on the farm into different compartments, whereby the BLV infected and non-infected are segregated. Due to the complex logistics, in many cases this cannot be implemented, but for some farms, this might be an option. We compared those options financially to a situation where no control was implemented. We assumed that in the latter case the prevalence will remain the same.

In this study we calculated the costs and benefits of BLV control over a ten-year period. All labour for the farmer and veterinarian was included in the calculations. The average within-herd prevalence in Alberta is 40%, and a herd size of 146 animals was used. Each cow that is infected with BLV will on average produce 3% less milk, will have a shorter lifespan or might leave the

herd prematurely. When leukosis develops, the carcass is condemned. Therefore, partial net revenue was assumed to be decreased by reduced milk production and reduced longevity of infected animals, as well as by development of leukosis and subsequent condemnation of affected carcasses. However, because Canada's dairy industry is based on a milk quota system, the revenue from milk sales was assumed to stay constant over time and not directly affected by BLV within-herd prevalence. Nevertheless, a farm's net revenue decreased due to indirect costs related to BLV-related reductions in milk production; these included the cost of additional feed and housing and maintaining more cattle to generate the same amount of milk as in an uninfected herd.

Some specific conditions were evaluated: 1) Transmission of BLV through colostrum to the calves is very important (will be discussed below). Pasteurization or freezing of colostrum or the use of dried colostrum are options to avoid transmission, but they have different financial consequences. 2) When farms are closed and replacements are not purchased, a new risk scenario is created, different from that in farms that regularly obtain animals without knowing whether the animals are BLV positive or negative. Therefore, also these different scenarios were evaluated.

These model-based calculations must always be interpreted with caution—no two farms are the same, and 'the average farm in Alberta' doesn't exist. Therefore, assessing if the cost calculation applies to your specific farm, with your specific management, is very important if we do not want to create unrealistic expectations.

In the present model, all considered strategies resulted in a positive net benefit after being implemented for at least four years. The 'test and segregate' strategy was the most beneficial. This was expected and can be explained by the highest rate of yearly reduction in prevalence, resulting in the highest net benefit, compared with the other strategies. Test and segregate control programs are highly efficient in preventing new infections, resulting in a rapid increase in income. While this strategy requires structural and organizational changes for dairy operations that might be difficult to implement, it offers an effective way of preventing new infections, when uninfected replacement animals are difficult to realize. We used a freestall situation as is found most commonly in Alberta. In the case of a tie-stall situation, the risk of infection and the cost and logistics of implementing measures such as test and segregate might be very different.

The short version of our conclusions was that all options that were evaluated are financially profitable. Naturally there is variation and some scenarios were more expensive than others but all the options lead to a higher net revenue for the farmer.

■ What Measures Can be Taken to Control BLV on a Dairy Farm?

Unfortunately, vaccination against BLV is not an option. None of the vaccine candidates that have been evaluated prevented the animals from getting infected. Therefore, we have to rely on other measures to control BLV. When testing for BLV and subsequently culling the positive animals is difficult to achieve, especially when the prevalence on farm is still very high and the test and segregate option is logistically challenging and too labor intensive, the focus shifts to implementing measures that can assist in reducing the number of infected cows on farm. When these measures are successful and have reduced the number of infected animals to only a few, culling might become feasible to remove the virus completely and therefore prevent the possible renewed spread of the virus.

There are several different transmission control measures that can be taken; a positive effect is that most of these measures assist in reducing the infection risk for other bacteria or viruses as well. So, when these measures are taken, we can expect that not only the BLV situation on farm will improve, but other microbes have less opportunity to establish themselves in the herd as well.

The most likely transmission routes are blood, colostrum and milk. Avoidance of transmission of these fluids from a positive animal to a negative will block the options for the virus to infect a new animal.

Blood can be transmitted through dehorning methods whereby blood vessels are opened, reuse of needles/syringes, reuse of examination gloves, breeding with a bull, hoof knives and other equipment that are not cleaned and disinfected between uses, and biting flies. The role of flies is always under debate and very unclear, but in theory it is possible that these insects transmit the virus.

One of the most important methods of transmission to a very susceptible part of the herd is using colostrum from BLV positive animals. Especially when colostrum from different cows is combined and the status of the animals is unknown, we should assume that the colostrum is infected and able to transmit the virus very efficiently. There are a couple of options to control the risk of transmission. The best and most reliable, but also the most expensive option, is pasteurization. An advantage of pasteurization is that it also reduces the risk of transmission of the bacterium that causes Johne's disease. A second method that can be considered, and is considerably cheaper, is freezing. During the Alberta winters this might be a very easy option, but also using a -20°C freezer will help reduce the risk of transmitting the virus. BLV is not a very strong virus and needs to be transmitted in combination with the earlier mentioned B-cells it replicates in. The idea is that freezing colostrum

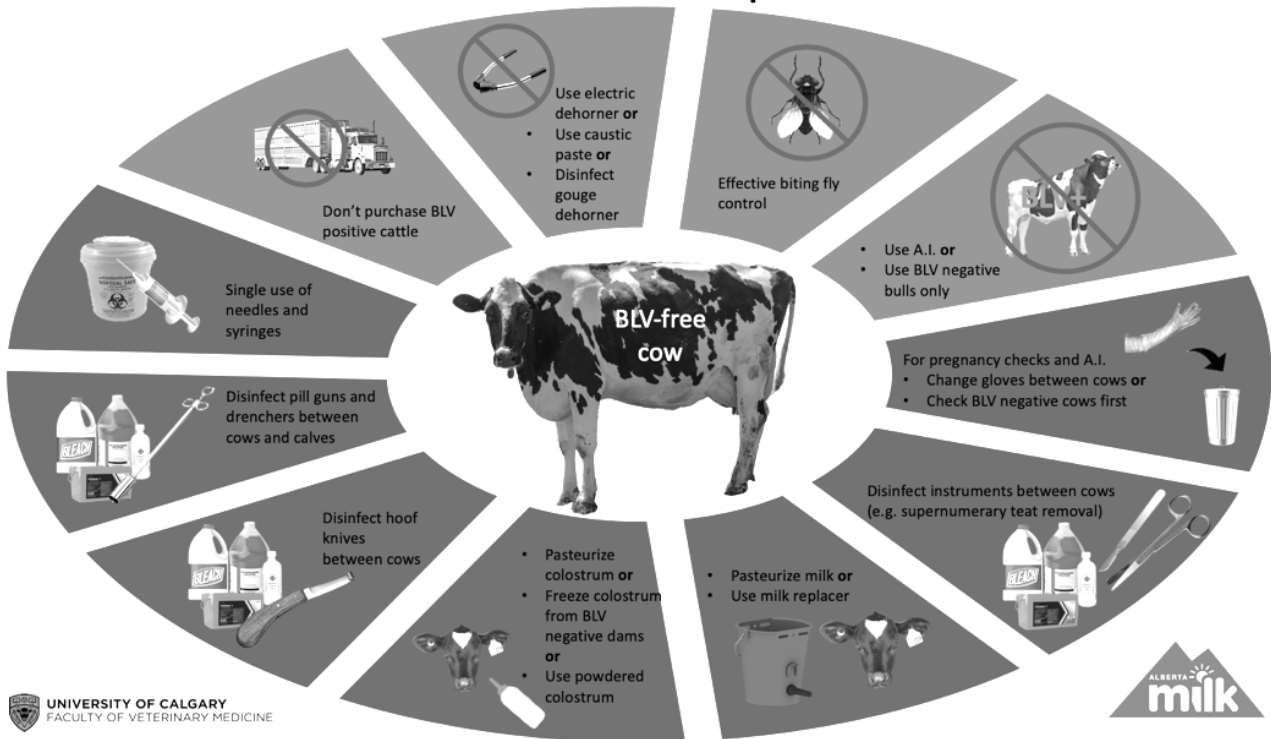
will disintegrate all the cells in the colostrum, therefore reducing the chance that BLV can be passed on to the calf. The use of dried colostrum is a very safe one, basically for the same reason as mentioned for freezing—there will be no live cells available anymore and so the virus doesn't have a chance to get transmitted. The same is true for milk—the use of milk replacer prevents virus transmission.

Last but not least, there is the possibility that a pregnant BLV positive cow will pass the virus to her calf. This happens in 10–15% of the pregnancies; this percentage increases to 40% in animals with a high proviral load. There are still a high number of calves that are born from BLV positive cows that remain virus negative.

All these options need to be considered when a complete control program will be rolled out on farm. Not everything can be implemented at the same time; therefore, it is important that farmers and veterinarians, together with other stakeholders, discuss the priorities of BLV control. This will be guided by the existing management of the farm, other disease control programs, the motivation of the farmer and his/her personnel to control BLV and other farm specific and management circumstances.

To aid farmers and veterinarians during the discussions about BLV control, the University of Calgary (Dr. Alessa Kuczewski and Molly Kavanagh) has developed a poster that has been distributed to all dairy farms and veterinarians in Alberta (Figure 1). In case farmers or others are interested in obtaining this poster, we can send a digital version when requested through: frank.vandermeer@ucalgary.ca.

BLV control is simple!



 **UNIVERSITY OF CALGARY**
FACULTY OF VETERINARY MEDICINE

For more information, visit <http://blv.msu.edu/> or contact Alessa Kuczewski (alessa.kuczewski@ucalgary.ca)



Figure 1: Poster that explains the main transmission routes of BLV

■ **First Experiences with BLV Control**

Currently a first trial of the control program has rolled out on 11 farms in Alberta. We are collaborating with the participating farmers to find out what the motivators and barriers are that enable or block the success of implementing and continuing a BLV control program.

BLV control is for farmers who are motivated to maintain these control measures for a long time. Farmers should not expect that BLV eradication is easy to reach or that there will be no setbacks. They are in it for the long term.

The improvement of animal health and welfare were the main drivers for dairy producers to participate in this trial. The producers also received encouragement from their herd veterinarian and their peers, and through constant reminders of the importance of control. The motivation was especially high for farmers with herds with a high BLV prevalence at the start, resulting in many dead cows with leukosis or animals with health issues because of BLV, both of which lead to economic losses. Farmers value their animals and understand that losses due to leukosis can be avoided. Some of the measures are relatively simple to implement and are inexpensive. However, increasing biosecurity on farm is not a temporary measure; it must be worked on all the time and the guard against bacteria and viruses needs to be up all the time. The University of Calgary has also developed a fact sheet that can be used to facilitate the discussion between dairy farmer and veterinarian (Figure 2). We hope it will be kept in the binder with important information for future reference.

BOVINE LEUKEMIA VIRUS (BLV)

BLV infection causes Leukosis

What you notice: ~5% of all BLV-infected animals develop tumors (=Leukosis)

What you don't notice: ~30% of all BLV-infected animals have an increased white blood cell count

All BLV-infected animals have a weakened immune system

Once infected with BLV, the cows are infected for life!

>90% of Alberta dairy herds are infected with BLV

ANIMAL HEALTH

BLV targets the white blood cells of the animals' immune system

↑ susceptibility to new infections

↓ response to vaccines

\$\$\$ ECONOMIC LOSSES \$\$\$

↓ Longevity
BLV positive cows are 23% more likely to be culled or die than BLV negative cows

↓ Milk Production
BLV positive cows produce ~3% less milk than BLV negative cows

Export restrictions on BLV positive cattle

Modes of transmission:



Figure 2. Fact sheet that can be used to facilitate the discussion between dairy farmer and veterinarian.

■ References

(all mentioned websites were accessed on December 6, 2018)

- Bartlett, P.C., B. Norby, T.M. Byrem, A. Parmelee, J.T. Ledergerber, and R.J. Erskine. 2013. Bovine leukemia virus and cow longevity in Michigan dairy herds *J. Dairy Sci.* 96:1591-1597.
- Buehring, G.C., H.M. Shen, H.M. Jensen, D.L. Jin, M. Hudes, and G. Block. 2015. Exposure to Bovine Leukemia Virus Is Associated with Breast Cancer: A Case-Control Study. *PLoS One.* Sep 2;10:e0134304.
- European Food Safety Authority, Panel on Animal Health and Welfare. Enzootic bovine leukosis. *EFSA Journal* 2015;13(7):4188. Available from: <https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2015.4188>. (Comprehensive review on BLV from a European perspective)
- Frie, M.C., and P.M. Coussens. 2015. Bovine leukemia virus: a major silent threat to proper immune responses in cattle. *Vet Immunol Immunopathol.* 163:103-14. (Scientific review discussing the impact of BLV on the immune system of cattle)
- Gillet, N.A., and L. Willems. 2016. Whole genome sequencing of 51 breast cancers reveals that tumors are devoid of bovine leukemia virus DNA. *Retrovirology* 13:75.
- Juliarena, M.A., C.N. Barrios, C.M. Lützelshwab, E.N. Esteban, and S.E. Gutiérrez. 2017. Bovine leukemia virus: current perspectives. *Virus Adaptation and Treatment.* 9 13–26. Available from: <https://www.dovepress.com/bovine-leukemia-virus-current-perspectives-peer-reviewed-article-VAAT>
- Michigan State University. Bovine Leukemia Virus. Available from: <http://blv.msu.edu>. (Significant source of information from MSU for farmers and veterinarians)
- Merck Manual; Veterinary Manual. Overview of Bovine Leukosis. Available from: <https://www.merckvetmanual.com/generalized-conditions/bovine-leukosis/overview-of-bovine-leukosis>. (General information of Bovine Leukosis available online)
- Office international epizootology. Enzootic Bovine Leukosis. Available from: http://www.oie.int/fileadmin/Home/eng/Health_standards/tahm/2.04.10_EBL.pdf (Specific information from OIE which include testing methods in detail).



