# Managing Genetic Recessives in Canadian Holsteins

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## Introduction

Within each breed association, there are various genetic recessives officially recognized for testing and reporting. This process provides important information for potential buyers of animals, semen or embryos and allows the breed association to monitor the degree of presence of each recessive within its domestic population with the goal of full elimination. For the Holstein breed, the World Holstein-Friesian Federation (www.whff.info), and therefore Holstein Canada (www.holstein.ca), officially recognize six genetic recessives for which carriers must be reported on pedigrees and other similar official documents including those available via the Internet.

**Table 1.** Genetic Recessives and Gene Codes for Holsteins.

| Genetic Recessive | Gene Code | Gene and Expression Codes[1] |
|---|---|---|
| BLAD *(Bovine Leucocyte Adhesion Deficiency)* | BL | BLC = Tested carrier of BLAD<br>BLF = Tested non-carrier of BLAD |
| CVM *(Complex Vertebral Malformation)* | CV | CVC = Tested carrier of CVM<br>CVF = Tested non-carrier of CVM |
| DUMPS *(Deficiency of Uridine Monophosphate Synthase)* | DP | DPC = Tested carrier of DUMPS<br>DPF = Tested non-carrier of DUMPS |
| Mulefoot *(Syndactylism)* | MF | MFC = Tested carrier of Mulefoot<br>MFF = Tested non-carrier of Mulefoot |
| Factor XI *(Bovine Factor Eleven Deficiency)* | XI | XIC = Tested carrier of Factor XI<br>XIF = Tested non-carrier of Factor XI |
| Citrullinaemia *(Bovine Citrullinaemia)* | CN | CNC = Tested carrier of Citrullinaemia<br>CNF = Tested non-carrier of Citrullinaemia |
| *Note 1: **C** = Carrier, **F** = Tested Free (Non-carrier)* | | |

The six genetic recessives that are officially recognized in Holsteins are listed in Table 1 with their associated gene and expression codes. For each disorder, a two-letter code has been established that is harmonized across all Holstein associations globally. It is important to remember these codes to identify the particular anomaly since tested animals will have the letter "C" added if they are identified as a carrier or the letter "F" added if they are shown to be a non-carrier (i.e.: free of the undesired gene).

## Data and Methods

All available pedigree data at Canadian Dairy Network (CDN) was used to establish genetic relationships among animals. Genetic test results, as received regularly from Holstein Canada, were used to identify known heterozygous carriers for each genetic recessive as well as for identifying animals that were tested to be free of the specific gene in question. For these animals, "Probability" values of zero (tested free) or 100 (heterozygous carrier) were assigned for each genetic recessive to reflect the probability of carrying a copy of the undesirable gene. For non-tested animals, a "Probability" value was computed for each genetic recessive taking into consideration the fact that all homozygous recessives cannot exist within the breeding population. For example, progeny resulting from the mating of two known heterozygous carriers have a 67% probability of being a heterozygous carrier for lethal genetic recessives, rather than the usual 50% likelihood. The calculation of "Probability" values can be broken down into three equations:

[1] $P_{Dom} = (200-P_{Sire}) \times (200-P_{Dam})$

[2] $P_{Carr} = [(200-P_{Sire}) \times P_{Dam}] + [(200-P_{Dam}) \times P_{Sire}]$

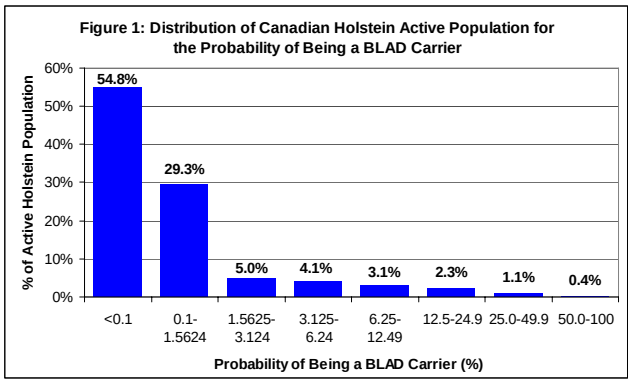
[3] "Probability" $= [P_{Carr} / (P_{Carr} + P_{Dom})] \times 100$

where $P_{Dom}$ denotes the percentage of the progeny resulting from a mating that are homozygous dominant and $P_{Carr}$ denotes the analogous percentage of those that are heterozygous carriers.

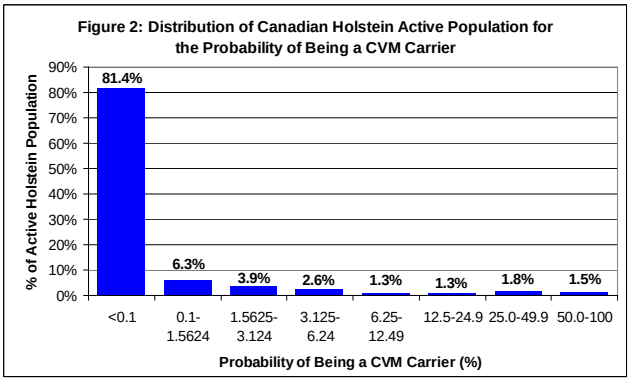
For each genetic recessive, once the "Probability" value was assigned or computed for all animals, trends in the frequency of carriers were plotted across birth years. In addition, a more detailed analysis of gene frequencies was conducted using the current active Holstein female population, which totals approximately one million animals including all cows on the herd inventory (i.e.: not culled) for herds on milk recording in Canada plus all herdbook registered heifers under the age of 30 months that have not yet calved for the first time.

## Recessive Description and Occurrence

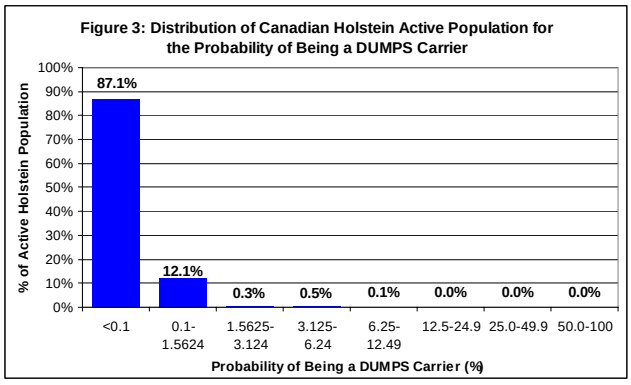
***BLAD*** is a lethal condition that is visibly expressed when the animal has received the gene from both parents. Affected calves have stunted growth, recurrent infections such as pneumonia, slow wound healing and die within the first year after birth. Osborndale Ivanhoe is the common sire in the pedigree of all affected calves. Since various proven sires that are known carriers of BLAD have been used to some degree within the Canadian Holstein population since the early 1990s, an analysis at Canadian Dairy Network (CDN) based on gene transmission probabilities (Figure 1) estimated that 1.28% of the current Canadian active Holstein female population are carriers of the BLAD gene (gene frequency of 0.64%), which spiked near 5% for heifers born in 1992 (Figure 5), but has steadily decreased since then due to strict testing programs for young sires entering A.I. in Canada.



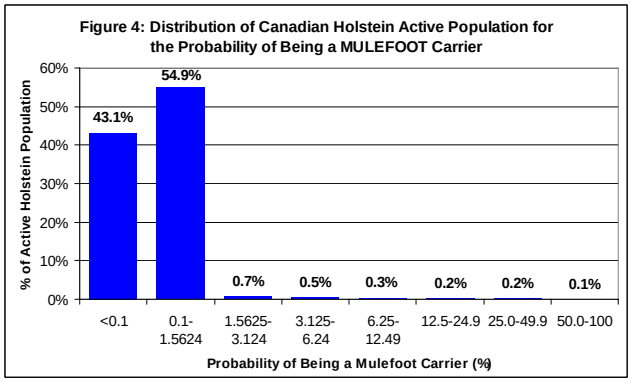

***CVM*** is also a lethal condition that occurs when both parents transmit the undesirable gene to the resulting progeny. In this case, however, expression occurs during pregnancy, which normally leads to embryonic death, abortion or the birth of a stillbirth calf with neck and leg deformities and often heart abnormalities. While Carlin-M Ivanhoe Bell is likely the most well-known CVM carrier, his sire, Penstate Ivanhoe Star, is considered to be the original source of this gene. Since most global A.I. companies immediately tested their battery of sires for potential carriers when the CVM gene was discovered in 2000, the CDN analysis on gene frequencies (Figure 2) estimated that 1.67% of the Canadian active Holstein female population are carriers of CVM (gene frequency of 0.83%), but the brief increase to near 2.5% for heifers born in 2001 or 2002 (Figure 5) was controlled by the immediate reaction of Canadian A.I. to eliminate carriers from their young sire testing programs.

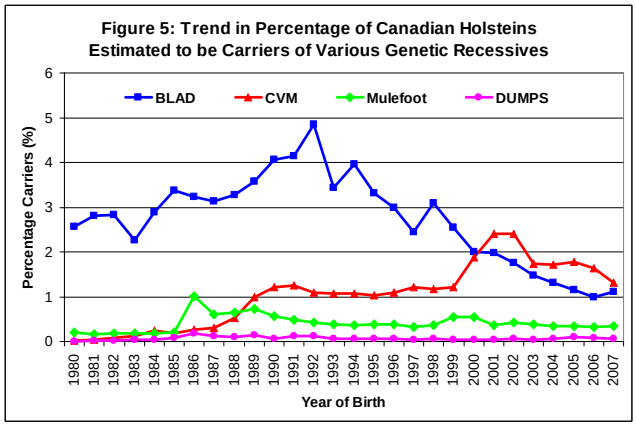



***DUMPS*** also leads to embryonic mortality when the gene is inherited from both parents but, contrary to CVM, the foetus always dies within 40 days after conception. This genetic disorder is caused by the deficiency of a specific enzyme important for the synthesis of DNA. Although only carriers can be found in the population, carrier females may require more breedings per calf born since some of their pregnancies could end in early embryonic death. DUMPS was discovered in the late 1980s with all known carriers tracing back to Skokie Sensation Ned. In Canada, due to the strict testing strategy implemented by A.I. companies, already more than a decade ago, the proportion of the Canadian active population that are carriers is estimated at 0.068% (gene frequency of 0.034%), which means that DUMPS has essentially been eliminated from the Holstein breed in Canada (Figures 3 and 5).




***Mulefoot*** is characterized by the fusion of the claws on one or more feet, with the front feet being affected before the rear feet and the right side before the left. As with the other genetic recessives above, affected animals must receive the gene from each parent. In the case of Mulefoot, however, the condition is not lethal and while affected animals have locomotive difficulties, they can live to reach maturity and beyond. In the Holstein breed, Wayne Spring Fond Apollo is commonly considered the original source of Mulefoot but, in fact, he inherited this defect from ancestors further back in his pedigree, namely Raven Burke Ideal and his dam, Raven Burke Elsie. Although a DNA test has recently been developed, which is not yet widely used in Canada, it is estimated that a very low percentage (0.364%) of the active Holstein population in Canada are carriers of Mulefoot (Figure 4). The slight spike in gene frequency for heifers born in 1986 (Figure 5) resulted from the arrival of second crop daughters of A Hurtgen-Vue Marathon once he was first proven in Canada in 1985, at which time he was not yet known to be a Mulefoot carrier.




***Factor XI*** (eleven) deficiency is a blood clotting disorder whereby affected animals show symptoms similar to haemophiliacs. While not a lethal condition, only animals that inherited the undesirable gene from both parents will express the symptoms. For these animals, haemorrhaging may occur at their birth from the umbilical cord, when being dehorned and/or when giving birth as an adult, which may result in death. Factor XI has only recently been officially recognized as a genetic recessive and therefore animals in Canada have not yet been formally tested for it. The originating source animal of this disorder in the Holstein breed has not yet been definitively identified.

***Citrullinaemia*** has also been recently acknowledged as a genetic recessive in Holsteins and, like others described earlier, it is lethal when the responsible gene is inherited from both parents. Calves that are affected cannot metabolize urea properly, which leads to high levels of ammonia in the plasma and ultimately in the brain. They consequently display neurological symptoms and rapidly deteriorate, leading to death within the first week of life. In Holsteins, Linmack Kriss King, has been identified as the source animal of this condition.

## True Red & White Gene

While not a genetic recessive gene, the pedigree analysis procedures used at CDN for the genetic recessives aforementioned were also applied to analyze the frequency of the gene responsible for the true Red & White coat colour in the Canadian Holstein population. In this analysis, carriers of the Variant Red (*VRC) or the Black Red (*BRC) genes were excluded since they are independent genes from that responsible for the true Red & White gene. Of course, an important distinction between the genetic recessive genes and the Red & White gene is that animals that are homozygous recessive for Red & White normally live and therefore facilitate the spread of the gene within the population. Recall that, for the genetic recessives discussed above, such animals died as embryos or early in life and would not reach the age of breeding.

For the true Red & White gene, the "Probability" values were assigned or calculated based on a combination of genetic test results and phenotypic codes on coat colour (i.e.: R&W or B&W). Animals with a phenotype of R&W were assigned a "Probability" value of 200 to reflect that it carried two copies of the recessive gene. Animals with a B&W phenotype were treated differently depending on whether they had a genetic test result available. Genetic test results identified B&W animals that were heterozygous carriers ("Probability"=100) or were proven to be non-carriers ("Probability"=0). For all other animals without an assigned "Probability" of 0, 100 or 200, the value was calculated based on the "Probability" values for their parents as outlined in equations 1 to 3 aforementioned.

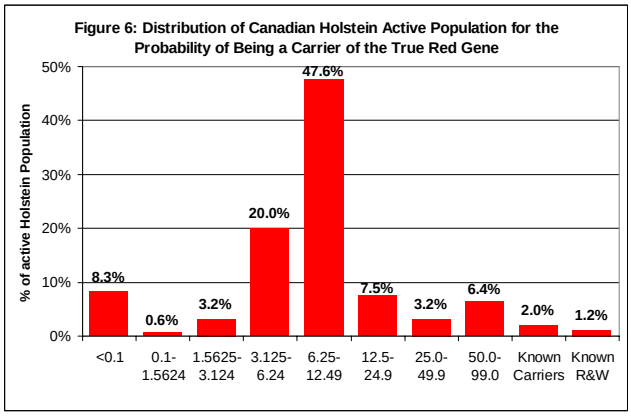
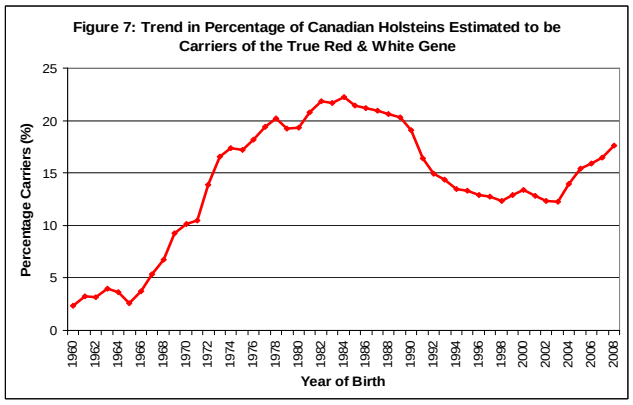



Figure 6 shows the distribution of Canadian active Holstein heifers and cows according to the probability of being a carrier of the true Red & White gene. Animals included in the last two categories, namely "Known Carriers" or "Known R&W" only include animals that have been officially designated with the appropriate genotypes and phenotypes by Holstein Canada. Similarly, a portion of the animals in the category with a probability level less than 0.1% are those animals officially identified by Holstein Canada that are not carriers of the Red & White gene, with the other animals receiving a calculated percentage that is below the 0.1% level. Overall, it is estimated that 12.65% of the Canadian active Holstein population are carriers of the true red gene and another 1.18% are homozygous recessive and show the true Red & White coat colour. This translates to an overall gene frequency in the Canadian active Holstein population of 7.51%.




Similar to Figure 5 for BLAD, CVM, Mulefoot and DUMPS, Figure 7 shows the trend by birth year of the percentage of Canadian Holsteins that are carriers of the true red gene. As expected, the presence of this gene in Canada was very low for animals born prior to 1970 but increased steadily to reach over 20% for birth years from 1981 to 1989 inclusively. Following a slow decline in the gene frequency during the 1990s, a regained interest in the selection for the true Red & White gene is visible for heifers born since 2004.

## Summary and Actions

There are currently six genetic recessives officially recognized by the World Holstein-Friesian Federation in the Holstein breed, which are briefly described in this article. Test results for these anomalies must be disclosed for presentation on official pedigrees and other similar documents. In Canada, data exchange procedures between Holstein Canada and

Canadian Dairy Network ensure that their respective web site also displays the appropriate codes for each animal with a genetic recessive test result. Producers and A.I. personnel should be familiar with the various gene and expression codes to avoid unintentional usage of carrier animals in their breeding program. The aggressive testing policies implemented by A.I. companies have been critical for the control and eventual elimination of these disorders.

The frequency of the true Red & White gene in the Canadian Holstein active population is estimated at 7.51% with an increasing trend for animals born since 2004. Nearly half of all Black & White animals have a likelihood between 6.25% and 12.49% of being a carrier of the true red gene. This partly comes from a regained interest in Red & White Holsteins but is also likely due to the increased frequency of genetically superior Black & White bulls and cows that are carriers of the true red gene.

In the future, CDN will be computing and publishing the estimated probability that each animal is a carrier of the true red gene to identify the most likely females to be mated to R&W or Red-Carrier sires for producers aiming to increase the frequency of Red & White animals in their herd. In the future, should new genetic recessives get discovered, probability values could also be published by CDN for use in mating programs to reduce the negative consequences associated with the fact that some known carrier sires may still be offered to Canadian producers.