NEW GENES: GOOD AND BAD

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I am going to start with the bad news first and then discuss a gene called the *slick hair* gene that may be useful in Florida dairies. The latest bad gene that the Holstein breed will need to deal with is called CVM, Complex Vertebral Malformation. This gene was discovered by researchers in the Netherlands and should be of concern to both commercial and purebred breeders of Holstein cattle. The gene has been found to be recessive in mode of inheritance as are the vast majority of the genes controlling genetic defects. What this means is that both cows and bulls can be completely normal and healthy but still be carriers of (heterozygous for) the defective gene. When such heterozygotes are mated together, there is a 25% chance that the calves born will be homozygous for the defective gene and thus express the abnormal condition. Usually this does not present a major problem unless bulls that are very popular and produce large quantities of calves via AI turn out, in retrospect, to have been carriers of a defective gene. This is exactly what happened in the case of the last major genetic defect, BLAD, Bovine Leucocyte Adhesion Deficiency, that surfaced about 11 years ago and now has largely been brought under control by DNA testing of the young sires entering progeny testing programs of the AI studs. In the case of BLAD, the bull almost completely responsible for its spread throughout the Holstein breed was Bell, Carlin-M Ivanhoe Bell, who has over 79,000 daughters with official production records in the USDA system and over 1200 sons with daughters in the system. A fact that is very surprising, almost shocking, to me is that this same bull, Bell, was also a carrier of this new genetic defect, CVM. In the case of BLAD, the defective gene was passed on to Bell from his grandsire, Osborndale Ivanhoe, through his sire, Pennstate Ivanhoe Star. It has now been determined that Ivanhoe Star was also heterozygous for CVM, probably having received it from his dam.

Since essentially all of the cows that Bell would have been bred to were homozygous normal for both the BLAD and CVM genes, it is unlikely that any of his hundreds of thousands of progeny were affected by either defect. However, when a bull is heterozygous for a defective gene, he passes it on to half of all his progeny. Thus, half of the progeny of Bell were heterozygous for BLAD, and half were heterozygous for this new defect, CVM. The diseases didn't start showing up until years later when male descendants of Bell were bred to his female descendants. Even then, in the case of BLAD, it wasn't immediately recognized as calves afflicted with BLAD appeared normal at birth and probably most of the affected bull calves were slaughtered for veal before they would have died from infections due to their defective immune system.

In some ways, CVM is similar to BLAD in that most (two-thirds or more) of the affected (homozygous for the CVM gene) calves will be reabsorbed as embryos or aborted as fetuses prior to the 260th day of gestation. Thus, the loss of these pregnancies would not have been likely to have led to suspicions of a single gene, genetic defect as the cause. The remaining one-third of pregnancies result in a stillborn calf, typically 1-2 weeks prior to the expected calving date. The most noticeable characteristics of CVM-affected calves are malformed legs with flexed and rigid pasterns, a shortened neck and an abnormal curvature to the spine. However, because the physical defects due to CVM can be so subtle, many affected calves and fetuses go unrecognized. Definitive diagnosis of CVM usually requires a necropsy or autopsy to detect the abnormal curvature of the spine, fused vertebrae and fused or missing ribs. Vertebral anomalies vary from severe to subtle and may require

radiographic studies or careful dissection of the spine to be distinguished. Thus, in many cases, such calves were probably born in U.S. herds but not recognized for what they were, calves homozygous for a single gene genetic defect. Calves showing the affects of CVM are shown in figures 1 and 2. While they appear somewhat abnormal in these photos, it is also easy to imagine that dairymen may not examine dead calves too closely, especially those born prior to term, and may overlook what are often subtle abnormalities.

In 2001, the NRS of the Netherlands announced its conclusion that CVM is caused by a single recessive gene. Their large-scale study of breeding records tracked more than 500,000 inseminations of cows that were sired by CVM-carrier bulls. The service sires included 38 CVM-carrier bulls and 77 non-carrier bulls. The services to CVM-carrier bulls resulted in 5.83 percent fewer live calves than were produced by services to non-carrier bulls. In addition, each of the 38 CVM-carrier bulls had a lower rate of live calves than any of the 77 non-carrier bulls. This analysis, coupled with the fact that the current DNA marker test has yet to find a live animal with a homozygous genotype, supports the NRS findings of a lethal when homozygous, recessive gene.

So, how serious of a problem is CVM? Well, the problem is not only that Bell sired so many daughters, but also that many of his prominent sons, including Elton and Southwind and others, also were heterozygous for the gene and sired many progeny. I have seen a figure quoted that due to the influence of Bell on the Holstein breed that the gene frequency of the CVM gene in the Holstein breed is from .04 to .05. If this estimate is correct, when we breed a CVM carrier bull to a Holstein cowherd of unknown parentage, the chance that a diagnosed pregnancy would result in a calf homozygous for CVM and thus would be either stillborn or aborted earlier is from 3.84 to 4.75% depending on whether we use .04 or .05 as the gene frequency of CVM in the breed. Because of this information I believe that it is critical that dairymen that know that they have used CVM positive bulls in their herds or do not know the pedigrees of their cows not use CVM positive (heterozygous bulls). The death rate in newborn Holstein calves is already around 10% and we don't need to do anything that we now know will increase it!

Now, at this point, I hope that I have convinced you that CVM should be an important concern to dairymen that are using Holstein bulls. The next relevant question is, what is the Holstein Association doing about it and what should you as dairymen do about it? The Holstein Association is approaching CVM in the same fashion as it approached BLAD; that is, to encourage DNA-testing of all AI sires and many cows and then identifying their genetic status through the use of suffixes on their names. Bulls that have been DNA-tested and are homozygous normal, that is not carriers of CVM, will have a suffix of TV after their names, while those that are carriers of CVM will have a suffix of CV. This will allow dairymen to choose only bulls that are TV if they have a number of daughters of CV bulls in their herds or do not know the parentage of their cows. You should be especially careful to avoid CV bulls if you know that you have used sons of Bell, or his sons, Elton and Southwind, that are known to be carriers of CVM. Some of the current sires known to be carriers of CVM that you may have young daughters of in your herd are listed in Table 1. You will note that all studs have bulls that are CVM carriers due to the widespread distribution of Bell breeding within the Holstein breed. A complete list of sires that have tested positive for CVM is available from the Holstein Association (http://www.holstein.com/).

To provide more information about sires that have played an influential role in the breed, the Holstein Association and NAAB have initiated a special program to test older (born prior to 1990), non-active bulls who have had a substantial influence on our current population. These two organizations are working together to identify the bulls, locate DNA and pay for the CVM testing. In

some cases, where semen is very scarce, the resources of the USDA's Cooperative Dairy DNA Repository will be utilized.

So, what are the bull studs doing about the situation? I found the following statements on the Genex website and felt that their approach to the problem was very appropriate. It is likely that all other studs using similar approaches.

The following measures have been recommended by staff and approved by the Genex board of directors:

- Label all active proven sires and consider CVM status when activating bulls for or removing bulls from the Genex sire lineup.
- In-waiting bulls will not be removed based on their CVM status.
- Stop sampling known CVM carrier young bulls, effective October 15, 2001. Any exception to this will need the approval of the Genex COO and the young sire will need to be clearly labeled as a CVM carrier. This decision is expected to cost the Cooperative $155,000 in bulls that will not be sampled. Although this sounds like a lot of money, it is the responsible thing to do and will assure the availability of a CVM-free sire lineup in the future.
- Potential carriers of CVM will be tested on the farm and only those testing negative for CVM will be purchased.
- Cows contracted for embryos must be tested negative for CVM or be at least four generations from a known carrier.

Adhering to this policy will mean that, in about one generation, Genex will basically eliminate CVM from its bull population.

As all studs use the same or similar procedures, in 7 to 10 years very few, if any, CVM positive bulls will be offered at stud and, to the extent that calves are sired by AI bulls, the gene frequency in the population as a whole will decline by 50% per generation. This assumes no female culling based on DNA testing. In the meantime, what should Florida dairymen be doing regarding CVM? Dairymen that use CVM positive bulls via AI or that use bulls via natural service will run the risk of losses due to abortion or stillborn calves due to CVM. By use of AI bulls that are TV, this loss can be avoided. If a natural service bull is going to be used, he should be DNA-tested for CVM if his 4 generation pedigree shows any evidence of Bell breeding. This is now much easier than it was several months ago as ImmGen, Inc., College Station, Texas has obtained the license to perform CVM testing. By sending a blood, semen or hair sample to ImmGen, Inc., it can be determined if an animal is heterozygous for the CVM gene or is homozygous normal. The charge for testing for CVM is $45 per sample. This is less than half the value of one newborn heifer calf that could be lost through the use of a CVM positive bull on a cow that is also a carrier. In order to insure that ImmGen has all the information needed to provide an accurate interpretation of test results, each sample or specimen should be accompanied by a record of identification form prepared by the Holstein Association.

Figure 1. A calf with CVM.

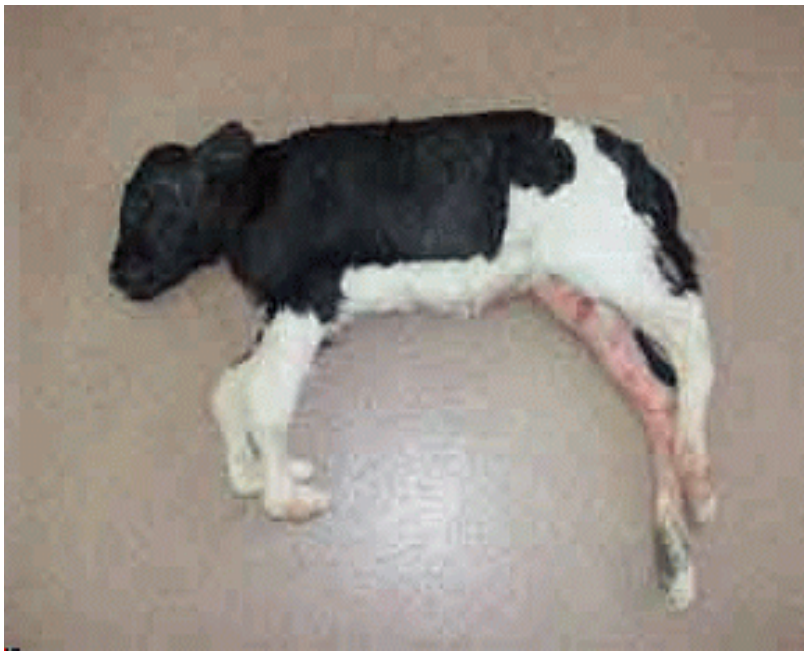

Figure 2. A second calf with CVM displaying similar malformations.

Table 1. A Sample of Superior Current Holstein Sires Reported* to carry the CVM Gene.

Bull name	AI organization	
FISCHER-HGHTS CORONATION	Alta Genetics	Mica X Elton^{CV}
SANDY-VALLEY BULLET	Alta Genetics	Duster X Bellwood
WA-DEL CONVINCER	ABSGlobal	Elton^{CV} X Cleitus
RICECREST LANTZ	ABSGlobal	Luke X Southwind^{CV}
RICECREST ROSCOE	ABSGlobal	Roebuck X Southwind^{CV}
WINDSOR-MANOR MACHOMAN	ABSGlobal	Rudolph X Elton^{CV}
PRIDE-OF-IOWA WILL CARL	ABSGlobal	Mark William X Mascot
KREGNOL JABOT JR	Accelerated	Jabot^{CV} X Aerostar
FARNEAR ELTON CREAM PHILIP	Accelerated	Elton^{CV} X Tesk
ANDACRES HUNTER ORION	Genex	Pontiac Hunter X Leadman
SANDY-VALLEY ADDIAS	Genex	Converse^{CV} X Mascot
HUNSBERGER ELTON COPPER	Genex	Elton^{CV} X Mark
KNOXLAND LABELLE C IDEA-	Genex	LaBelle^{CV} X Mountain
MR POTTERS-FIELD JAY 95	Genex	Pontiac Hunter X Liberty^{CV}
VAN-ACRES SHADY-WAY NIKE	Genex	Duster X Slocum
GLEN-TOCTIN TERRELL	Genex	Marconi^{CV} X Mascot
PARADISE-R CLEITUS MATHIE	Select	Cleitus X Bell^{CV}
REGANCREST ELTON DURHAM	Select	Elton^{CV} X Mark
RICECREST BRANDON	Select	Belltone^{CV} X Blackstar
PECKENSTEIN ELTON CURTIS	Select	Elton^{CV} X Thor
CATALINA MATHIE MAGNUM	Select	Mathie^{CV} X Elton^{CV}
NORS C EMORY CALVIN	Select	Emory X Highlight
GLEN-D-HAVEN RUDOLPH JETTA	Select	Rudolph X Blackstar

*The bulls listed are samples of those listed as CVM positive on the Websites of the AI studs listed. All stud websites that I examined announced bulls that were CVM carriers.

The Slick Hair Gene

A gene which has a potentially useful impact on Florida dairy production is the *slick hair* gene. This gene is being studied here in Florida and has been studied elsewhere because of its impact on heat tolerance. The *slick hair* gene causes cattle to have a hair coat similar to that of an animal that has just been clipped. In Figure 3 you can see Carora, Venezuelan Brown Swiss composite crossbred cattle with and without the *slick hair* gene. Animals with slick hair have been found to maintain a rectal temperature under heat stress that is 0.5E C lower that animals of the same breed composition, but with normal hair. Holstein cattle with slick hair were located several years ago in Puerto Rico. The owner of these cattle (called "pelonas" in his herd) is convinced of their superiority to normal-haired cattle under his management system which relies almost totally on grazing. He told me that if a heifer was born as a pelona, "He knew that they were going to be good." I asked him if the pelonas were more heat tolerant than normal-haired Holsteins and his response was, "I don't know if they are more heat tolerant, I only know that they are more productive." An evaluation of his DHIA records supports his statements as the pelonas had a first lactation herdmate deviation of 3511 pounds, which is over 25% of the herd average. While this figure is based on only 6 first lactation cows, these cows have been in his herd for many years. The owner, Mr. Borges, remembers his grandfather buying a black and white spotted cow with this type of haircoat over 30 years ago. Apparently all the pelonas in his herd descend from this cow. The *slick hair* gene, being dominant in mode of inheritance, has persisted in this herd in spite of 30 years of mating with registered Holsteins. We are currently working with some of the genetics from this herd as well as with cattle descended from Senepol crosses. We now have calves that are about 7/8 Holstein, some of which may be homozygous for the *slick hair* gene. Also, we have pregnancies that will produce 7/8 Holstein calves at a large cooperating dairy in the Okeechobee area. Perhaps most exciting, however, is the work of Dr. Karen Moore of our department who is working to clone one of the slick-haired Holstein cows in the Borges herd. This cow is of very correct type and is the highest producing Holstein cow in this herd, producing a peak production on almost exclusively grazed forage of over 100 pounds per day! We also are exploring the possibility of importing this cow so as to facilitate collection of embryos from her sired by the best U.S. Holstein bulls.

Another potential genetic resource that I am examining is the Reina breed of Nicaragua. Reina cattle are tropically adapted dairy cattle. They are red in color and are slick-haired. Cows of this breed produce up to 7,000 pounds of milk a year on forage alone while also raising a calf. My interest in these cattle is also based on the potential for use as a breed to use for crossbreeding with Holsteins. This cross would not only yield the heterosis that comes from having a crossbred animal (as expressed in increased calf survival and improved fertility and perhaps, longevity), but also heat tolerance through incorporation of the *slick hair* gene into the cross. Since the Reina is a dairy animal with adequate udder traits, their crosses with Holstein should be quite acceptable in type and perhaps be exceptional for use in grazing dairies.

The question that remains to be answered regarding the *slick hair* gene is what will its advantages be in Florida dairies, using grazing or conventional drylot feeding? A preliminary study conducted on 3/4 Holstein cows in Venezuela indicated a significant advantage in days open and milk yield under drylot conditions in a very dry environment. We might expect an even greater response in humid Florida where heat stress is likely greater. Under summer conditions in Florida, the ability of a cow to maintain a lower body temperature may improve demonstration of estrus and, especially, embryo survival.