

A Different Kind of Haplotype...

HCD: Haplotype associated with Cholesterol Deficiency

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What is HCD?

This summer, German researchers discovered a new haplotype in the Holstein breed that is unlike the previously found haplotypes impacting fertility. This haplotype, called “HCD” (Haplotype associated with Cholesterol Deficiency), leads to chronic diarrhea in calves that does not respond to treatment, as well as other illnesses. The blood of affected calves, those that inherited the problem gene from both parents, showed a cholesterol deficiency that prevented the normal deposition of fat in body tissues.

HAPLOTYPE: A short section of the genome transmitted as a block of DNA from parent to progeny.

GENE: A specific sequence of DNA controlling a trait or characteristic.

Cholesterol is a modified steroid and a fat molecule that is an essential component of all cell membranes. It is also used to build steroid hormones, bile acids, vitamin D and the protective shell around nerves in the brain. Cholesterol is important for reproductive hormones, digestion and the nervous system and while a low level of cholesterol is survivable, a severe deficiency will lead to illness and death¹.

Who is at Risk?

The specific gene that causes HCD has not been identified but German researchers found a haplotype consistently present in carriers. By analyzing pedigrees, the researchers revealed that all carriers of HCD trace back to *Maughlin Storm*. The haplotype found in *Storm* carrier descendants also exists in *Willowholme Mark Anthony* since the two bulls have a common ancestor – *Fairlea Royal Mark*. The complicating factor, however, is that *Mark Anthony* carries a non-defective version of the haplotype, meaning his offspring with two copies of the haplotype go on to live normal lives. This led researchers to the conclusion that the mutation causing HCD must have occurred in the generations between *Royal Mark* and *Storm*. The table on the next page lists key HCD carrier sires with over 5,000 registered daughters in Canada.

¹The Great Plains Laboratory Inc. Cholesterol deficiency: a major factor in many chronic disorders. GPL4U.com

HCD Carrier Sires with over 5,000 Registered Daughters Born in Canada		
RELATIONSHIP TO MAUGHLIN STORM (HOCANM5457798)		
SONS	GRANDSONS	GREAT GRANDSONS
Pursuit September Storm Comestar Stormatic Hartline Titanic-Et Ladino Park Talent-Imp-Et	Braedale Goldwyn Gillette Final Cut Dudoc Mr Burns Kerndt Stallion	Gillette Windbrook Comestar Lauthority Gillette Stanley Cup Lirr Drew Dempsey Comestar Lavanguard Golden-Oaks St Alexander-Et Gillette Windhammer

Since the gene for HCD is unknown, the only way to identify carriers is by using the haplotype. HCD status is easy to determine for animals with only *Storm* in their pedigree, but is more difficult if both *Storm* and *Mark Anthony* appear.

The frequency of HCD haplotype in the Canadian Holstein population peaked for heifers born in 2012 and has been decreasing since then, even before HCD was known. This is due to a shift in bloodlines used to produce sires that have entered A.I. in recent years. The graph shows the percentage of carriers (1 copy or 2 copies of the HCD haplotype) in the Canadian Holstein population of heifers by year of birth. For example, in 2014 and 2015 around 13% of the heifers born in Canada are estimated to be carriers of HCD. Heifers that carry two copies will die due to cholesterol deficiency. Those that carry one copy should not be mated to male HCD carriers as 25% of the time offspring from the mating of two carriers will result in a calf affected by cholesterol deficiency and will go on to die before reaching 6 to 8 months of age.

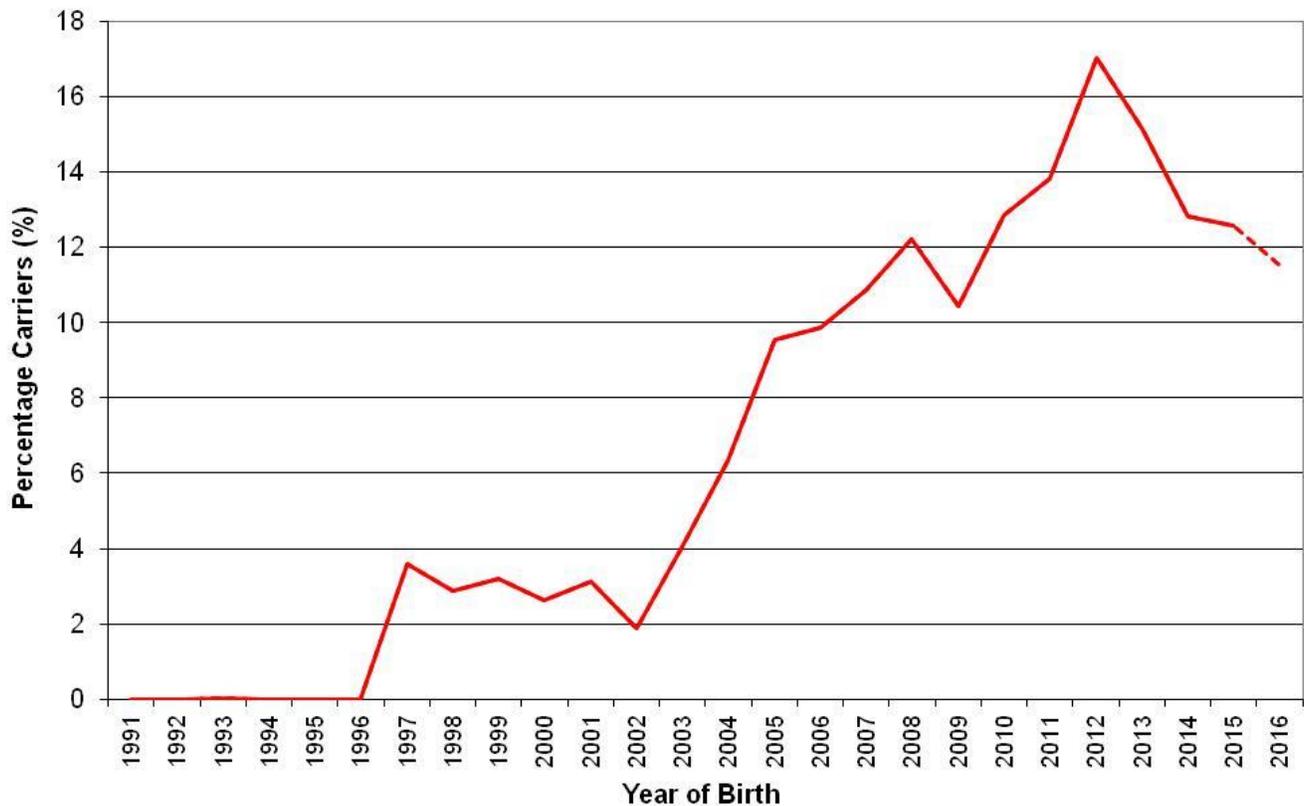
Symptoms of HCD in Calves:

- Going off feed
- Weakness
- Weight loss
- Chronic scours

There is no treatment for HCD and calves usually die within 3 weeks to 8 months of life.

A recent analysis by CDN of breeding data during 2015 showed that 90% of all breedings were done with semen from sires known to be free of HCD (non-carriers). From this same data, we expect only 1 out of 300 calves born during 2016 to be affected by HCD and suffer early calf mortality.

Trend in Percentage Carriers of HCD in Canadian Holstein Females



How to Test for HCD?

The only way to determine if an animal has HCD (carries 2 copies of the haplotype) or is a carrier (with only one copy) is through genotyping, which will also yield a genomic evaluation. CDN calculates HCD Carrier Probabilities, in other words, the likelihood an animal carries the undesirable HCD haplotype. These are displayed on the animal's Pedigree tab on CDN's website, as seen in the image on the next page.

Determining HCD:

- Only genotyping can tell if an animal is a carrier or has HCD
- Vets can test blood serum samples for cholesterol level to determine if a deficiency is present

MAUGHLIN STORM

[GenoTest Form](#)

[Breed Association](#)

Summary Genomics Prod. Type Functional Mastitis Calving Progeny **Pedigree** Inbreeding

Pedigree Tree

HOCANM5457798	MAUGHLIN STORM Ⓒ	STORM
0073HO02012	ET BW CVF BRC BLF HH: 1%, 1%, 1%, 1%, 1% HCD: 99%	Born 26-AUG-91 1.35%INB 17%R

- A 99% is displayed if an animal is identified as a carrier, which reflects the fact that the haplotype analysis is essentially, but not perfectly, 100% accurate.
- A 1% is displayed if an animal has been identified as Free.
- An animal that hasn't been genotyped or has both *Storm* and *Mark Anthony* in their pedigrees may have estimated Carrier Probability between 99% to 1%, depending on the probability values of its parents and other relatives.
- Animals with two asterisks (**) next to the HCD Carrier Probability are expected to carry two copies of the gene and die within the first 6-8 months of life.

What's Next?

Genotyping allows for the discovery and control of genetic anomalies like HCD. The impact of these haplotypes can be eliminated by avoiding the mating of carrier sires to carrier females, which is best achieved using A.I. mating programs. Carrier Probabilities for both males and females are shared in data files with all major A.I. companies.

Herds with a significant presence of red carriers should pay particular attention to controlling HCD since *Mr Burns* and *September Storm* bloodlines (both carriers) are more likely to be represented. In addition, herds using bulls for natural service should genotype potential herd sires if Storm, or any known carrier descendant of *Storm*, appears in the animal's pedigree in order to eliminate the possibility of using a herd sire that carries HCD.

On a broader scale, the discovery of HCD highlights the importance of producers reporting to DHI the date and reason for every animal leaving the herd, including young calves.

Planning Breeding:

- Mating programs with major A.I. companies have data to prevent problem crosses
- CDN calculates carrier probabilities for genotyped animals

For more information on HCD please contact:

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