

Genomic tools help us manage genetic defects

John Cole for *Progressive Dairy*

AT A GLANCE

Genetic defects result from errors in biology that we can't control; however, new tools that help us identify these defects and genomics are a key in managing them.

There is perhaps nothing more discouraging on the farm than visiting the maternity pen and finding a calf that displays an abnormality, such as being unable to stand. Developmental defects like this can be caused by something in the environment that disrupts the normal developmental process, such as contaminated feed or an intrauterine infection. Other times, they're caused by changes in an animal's DNA that can be passed on from parent to offspring.

Genetic defects have the potential to spread rapidly in a population if an influential animal is not a known carrier. For example, the APAF1 mutation associated with Holstein Haplotype 1 (HH1) arose in the bull Pawnee Farm Arlinda Chief (040HO025), which was widely used. While environmental factors can also be problematic in defect development, this discussion will focus on genetic defects.

Mutations are biological

The most common genetic defects are caused by a single change in an animal's DNA. For example, HH1, which causes embryos to die, is the result of a single DNA "letter" (one half of a base pair) changing from a C to a T in a gene named APAF1. This change causes the gene to end before it's supposed to, and when it's

not available in its complete form, the embryo dies.

However, some mutations are more complex. Holstein cholesterol deficiency (HCD), for example, is caused by the insertion of 1,300 base pairs into a gene named APOB. This disrupts the protein made by that gene. A defect like HH1 can spread widely throughout the population because early embryonic losses aren't easily detected without genomic information. Unlike HCD, which results in sickly calves that are often euthanized, the presence of HH1 just looks like a cow didn't get pregnant when she was bred. These two examples also represent the extreme economic impacts genetic defects can have, with early embryonic losses being the least expensive and defects affecting live calves being the most expensive.

Genetic defects result from errors in biology that we cannot control, so the presence of a genetic defect in a herd is not a sign of incompetence or negligence. New conditions aren't the result of a mistake and are beyond an individual farmer's control.

Are there more genetic defects now?

Many people have commented that there seem to be a lot more genetic defects than there used to be, but that's not really true. **Figure 1** shows the number of new genetic defects identified from 1893 to 2024 as reported in the Online Mendelian Inheritance in Animal Database. The average over all this time is one new defect identified per year. However, something important did happen in 2011.

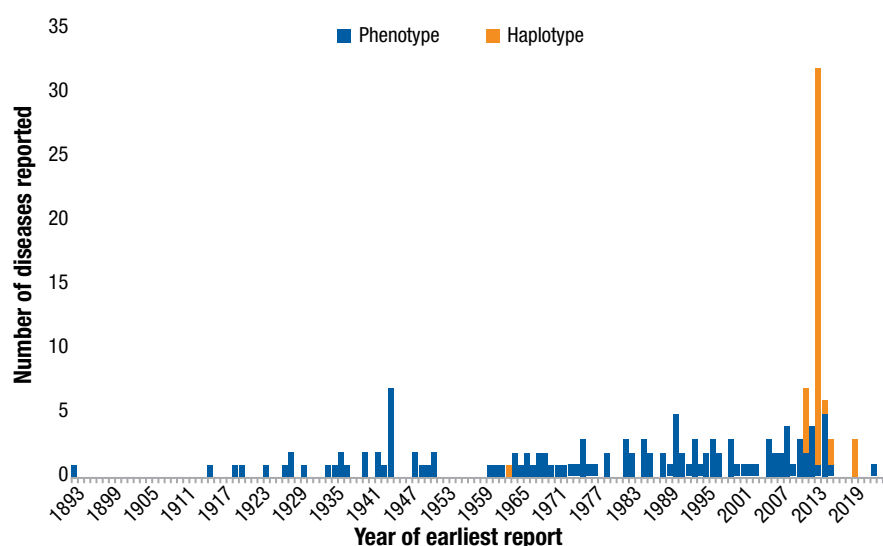
The number of genotyped animals, especially cows, rose rapidly after the first genomic predictions were

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Additional resources

- CDCB Haplotypes and Genetic Conditions website: <https://uscdcb.com/haplotypes/>
- "Invited review: Management of genetic defects in dairy cattle populations" by Cole et al. in *Journal of Dairy Science*: [www.journalofdairyscience.org/article/S0022-0302\(25\)00109-2/fulltext](http://www.journalofdairyscience.org/article/S0022-0302(25)00109-2/fulltext)
- World Holstein Friesian Federation Genetic Traits and Carrier Codes Fact Sheet: <https://whff.info/wp-content/uploads/2024/11/Genetic-Traits-and-Carrier-Codes-fv-2024.pdf>

FIGURE 1 The number of Mendelian diseases of *Bos taurus* cattle reported by year from 1893 to 2024



Defects were identified based on phenotypes ("Phenotypes", blue bars) reported from the field or using a deficiency-of-homozygotes approach ("Genotypes", orange bars).

Source: Cole et al., 2025

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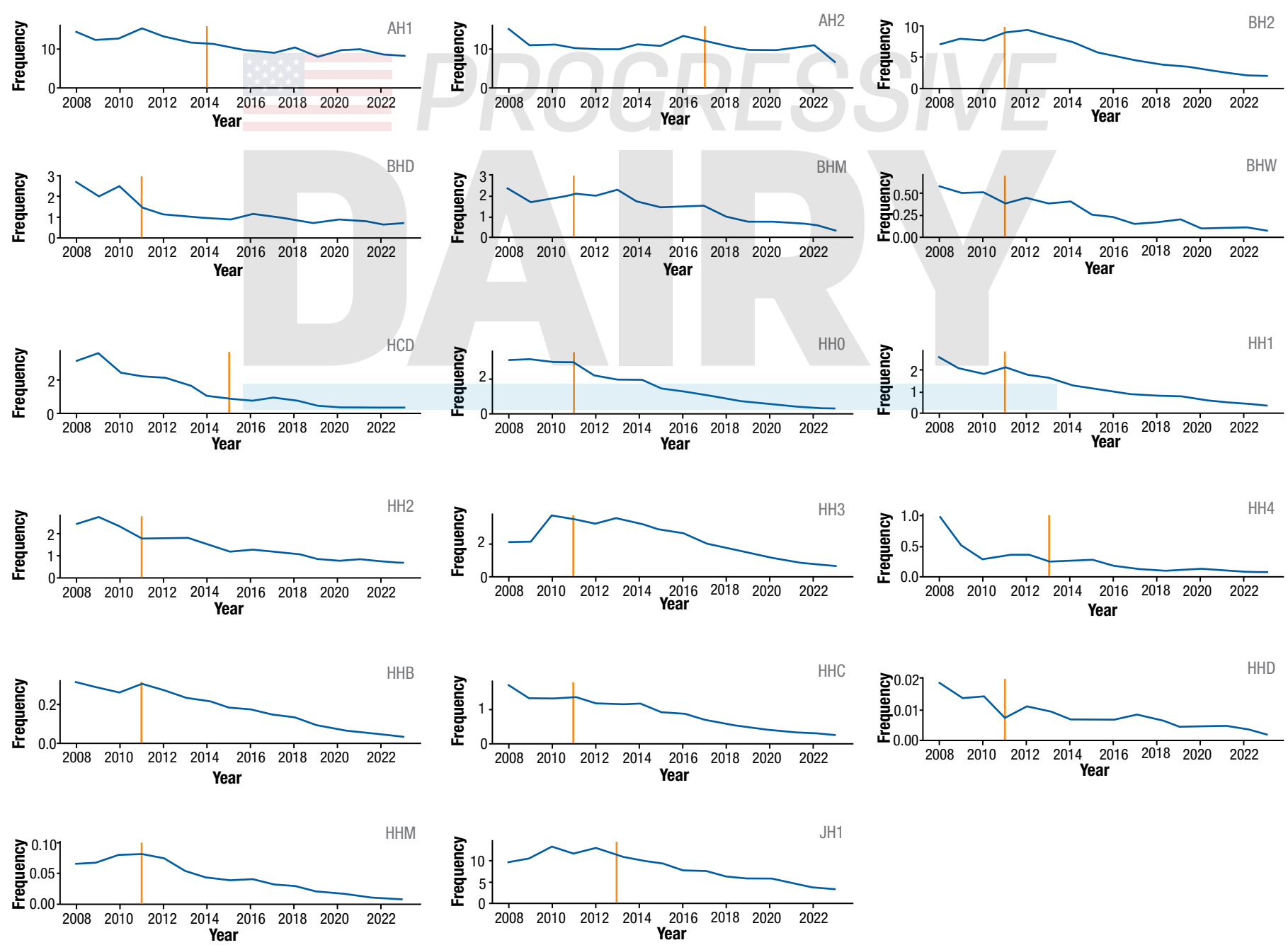
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FIGURE 2 Haplotype frequencies by year (2008-2023) for several recessive genetic defects in U.S. Ayrshire, Brown Swiss, Holstein, and Jersey cattle tracked by the Council on Dairy Cattle Breeding



The vertical orange line indicates the year each haplotype was first published. AH1 = Ayrshire haplotype 1, AH2 = Ayrshire haplotype 2, BH2 = Brown Swiss haplotype 2, BHD = Spinal dysmyelination, BHM = Spinal muscular atrophy, BHW = Weaver, HH0 = Holstein haplotype 0, HH1 = Holstein haplotype 1, HH2 = Holstein haplotype 2, HH3 = Holstein haplotype 3, HH4 = Holstein haplotype 4, HHB = bovine leukocyte adhesion deficiency, HHC = complex vertebral malformation, HHD = deficiency of uridine monophosphate synthase, HHM = mulefoot, and JH1 = Jersey haplotype 1.

Source: Cole et al., 2025

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introduced in 2009. Scientists at the USDA’s Animal Improvement Programs Laboratory (now the Animal Genomics and Improvement Laboratory) then determined how to identify previously undetectable genetic defects by using genomic information. These were conditions like HH1 which were very difficult to identify before genomics since they cause embryos to die early in pregnancy, appearing simply as an unsuccessful breeding. This method was quickly adopted in other countries and applied to many different breeds, leading to the notable spike of new defect reports in 2013.

After that initial era of discovery, things have settled back down to the historical average. The reason it seems like there are more genetic diseases now than in the past is that new technology now allows us to identify things that we couldn’t before. It’s better to know about something that can be managed than to not know about it at all.

Testing options

So how can we manage these defects? The gold standard is a genetic test, which is a laboratory assay that tells us definitively if an animal is a carrier of a particular defect or not. These laboratory tests are available for most of the known defects in our cattle populations today, but they’re not available when new defects are first discovered. Most laboratory tests are very good – the false negative and false positive rates are both low – but sometimes they’re not. This usually comes down to the underlying biology of the defect – a single-base change in an animal’s DNA is usually simple to detect, but sometimes the mutation is caused by a larger change in the DNA or more than one gene is involved in its expression.

There is often a lag between when researchers identify the cause of a new genetic defect and the availability of a genetic test. If a gene test isn’t yet available, there may be a haplotype test that can be used to determine

the carrier status of genotyped animals. It is important to understand that gene test results won’t change unless a laboratory error was made, but haplotype results do sometimes change as new information becomes available.

The best way to manage genetic diseases in your herd is to avoid using bulls that are known carriers as much as possible and to genotype your cows so you know their carrier status before mating them.

Where are we today?

In a recent publication in *Journal of Dairy Science*, we reported that the economic impact of known genetic defects in the U.S. has fallen by about two-thirds since 2016. This is the result of lots of hard work by A.I. companies, breeders and dairy farmers to develop and use elite genetics that are free of known defects.

Figure 2 shows the change in haplotype frequency over time for several recessive genetic defects

tracked by the Council on Dairy Cattle Breeding (CDCB). The trends for each of these conditions is favorable. After the haplotypes were identified (shown by the vertical red lines), the frequencies steadily – and sometimes dramatically – declined over time. This proves that we can successfully manage our populations to improve their genetic health.

Notably, detection is the key to this progress. Currently, there’s no single organization that serves as a universal point of contact for reporting genetic defects in the U.S. If you are a member of a national breed association, share any abnormalities on your farm with them. You may also contact CDCB as the industry works together to limit the stresses these biological conditions have on our farms.

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