WHAT IF A SIMPLE DOMINANT GENETIC DISEASE AFFECTED THE AMERICAN ESKIMO DOG?

The Weather Channel has a series entitled *It Could Happen Tomorrow* which studies disasters (hurricanes, tornadoes, wildfires, etc.) striking a populous city, such as a Category 5 hurricane striking New Orleans (produced the year before Katrina); Houston/ Galveston (produced one month before Ike); and New York City (produced three years before Sandy). Weather disasters are not a matter of *if* but *when*.

Each episode begins with a piece entitled *It Did Happen*, a story about a terrible disaster which previously occurred, maybe 10 or even 100 years ago, or in a different city. The historical disaster is summarized and explained in terms of modern science to demonstrate what actions/events made the disaster deadly. The end of that piece leads into the "what if", as in *What if a Category 5 hurricane were to hit New York City today?*

The AEDCA Health Committee is providing real-life *It Did Happen* stories involving genetic diseases. Our first study takes us to the American heartland in horse country. Many dog fanciers are also "horse people", too, and some of you may even own Quarter Horses and be aware of this disease.

It Did Happen: THE AMERICAN QUARTER HORSE

On April 15, 1968, a chestnut Quarter Horse foal was born. Although he had Thoroughbreds on both sides of his pedigree, he was the living example of everything that a Quarter Horse was supposed to be. Originally bred to work cattle in semi-arid South Texas, the Quarter Horse must be muscular to stand up to the rigors of keeping cattle taut on the lariat; agile and nimble to cut a calf and keep it from the herd; and fit to run chasing cattle in the brush all day. The young chestnut colt was named Impressive- and he was!

The colt changed hands several times and even raced on the track until in 1974 at the age of six he became the first World Champion Open Aged stallion in the history of the breed with 48 halter points. He sired almost 30 World Champions and a total of over 2250 foals. One son, Noble Tradition, was a four-time World Champion stallion and a highly successful stud in his own right. In 1992, 13 of the top 15 halter horses were descendants of Impressive. In 1993 he was estimated to have in excess of 55,000 living descendants including Quarter Horses, Paints, Palominos, and Appaloosas (the last three breeds allow registrations of Quarter Horses or Quarter-crosses). Although Impressive died on March 20, 1995 (almost 28 years old!), his name still lives on today- although perhaps not as his fans would have imagined all those years ago when he was winning in the show ring and producing in the breeding shed.

Even as Impressive was still in high demand as a sire and commanding historically-high stud fees for his time, owners of his foals began to notice strange muscle twitchings that often left their horses unable to move. These episodes varied in duration and severity and were usually misdiagnosed as "tying-up" syndrome or colic. Today we know that these were the first cases of the disease Hyperkalemic Periodic Paralysis, or HYPP.

HYPP is a muscular disease which affects horses and humans caused by a genetic mutation that disrupts sodium channels, the gateway to the membrane of muscle cells. The disruption causes a series of cascading biochemical imbalances which result in stiffness, twitching, trembling, and profound muscle weakness which can cause paralysis and even death.

Impressive was still in demand as a stud horse and his offspring were still winning in the show ring as talk of the strange symptoms started to float around the Quarter Horse world. No one wanted to implicate the top stallion in the history of the breed, his well-known owner, and most especially the attorneys. So much money and prestige

was at stake that no one dared discuss the situation. After all, no one could actually *prove* that this disorder could be traced to Impressive.

Through funding provided by the American Quarter Horse Association (AQHA) and the University of California- Davis (UC-D) Equine Research Laboratory, medication was developed which along with diet to control the symptoms. Some owners decided that HYPP was merely a nuisance and didn't seem to care about its effects on their horses and breeding programs. However, most owners were blissfully unaware of the disease.

Using molecular genetics, researchers at UC-D were finally able to identify the culprit, a mutant gene; and they developed a blood test to identify which horses carried the mutant gene. UC-D's legal staff finally gave their approval to publicly identify "Horse Zero" as Impressive, which gave the disease the common name of "Impressive Syndrome".

The other shoe fell when researchers determined that the disease is inherited as an ***autosomal dominant*** trait, meaning that a horse would be affected if it inherited only one allele from either parent. Quarter Horse breeders use the letters H (HYPP) and N (normal) to designate the two alleles in the critical gene. Heterozygous HYPP horses (HN) carry only one copy of the mutant allele; but because the H allele is dominant over the Normal allele (N), the disease is expressed. Homozygous HYPP horses (HH) appear to show symptoms earlier in life and perhaps have more severe cases, but the disease in heterozygous Affecteds is just as devastating to the Quarter Horse gene pool.

Let's look at some possible matings of HYPP horses and their resulting offspring:

1. Homozygous Affected (HH) mated to a homozygous Normal (NN)- All offspring are heterozygous Affected (HN) and will have the disease.

	N	N
H	HN	HN
H	HN	HN

Obviously a homozygous Affected horse (NN) is devastating to the breed because even when bred to a genetic Normal (NN), all of its offspring will be Affected.

2. Heterozygous Affected (HN) mated to a homozygous Normal (NN)- Half of the offspring (50%) will be heterozygous Affected and will have the disease; and half (50%) will be homozygous Normal.

	N	N
H	HN	HN
N	NN	NN

3. Heterozygous Affected (HN) mated to a heterozygous Affected (HN)- Matings of heterozygous animals produce the greatest variation in offspring. One-fourth (25%) of the offspring will be homozygous Affected (HH); half (50%) will be heterozygous Affected (HN); and one-fourth (25%) will be homozygous Normal (NN). The end result is that 75% of the offspring (25% as HH plus 50% as HN)will have the disease.

	H	N
H	HH	HN
N	HN	NN

The genetic test was made available to owners and breeders in 1992. Still many breeders refused to acknowledge the potential effects that this disease could have on their breed. Finally at their 2004 convention, the AQHA passed motions to protect their beloved breed.

As of 2007 the AQHA requires genetic testing for any Quarter Horse foal which has Impressive or any of his descendants in its pedigree. The AQHA will no longer register any horse which is a homozygous Affected (HH) because all of their offspring will be Affected, no matter the mate. The status of heterozygous Affected horses (HN) is pending further discussion in the future as these horses can produce Normal offspring if bred to Normal (NN) mates. The AQHA does not appear to have any restrictions on breeding two heterozygous Affected horses, although common sense and ethics would seem to take that option away from responsible breeders due to the possibility of producing homozygous Affected offspring.

This disease in the Quarter Horse goes beyond the AQHA into other registries including the Appaloosa Horse Club (ApHC), the Palomino Horse Association (PHA), the Palomino Horse Breeders of America (PHBA), and the American Paint Horse Association (APHA). These registries all allow the registration of certain Quarter Horses meeting specific requirements. Those registries will need to make their own decisions regarding horses which are descended from Impressive.

Could such a scenario happen in the American Eskimo Dog? Would our reaction as breeders and owners be the same- that no one dares to speak out because of the very real fear of being sued? Would we take 12 years to take action once we had the tools necessary to evaluate our breeding stock? The answers to the first question is YES, an autosomal dominant disease could affect the Eskie. The answers to the other questions is up to the individual owners and breeders, but the Health Committee wants to do everything that they can to ensure that the AED community acts quickly to identify, halt, and prevent genetic disease from harming the future of our breed.