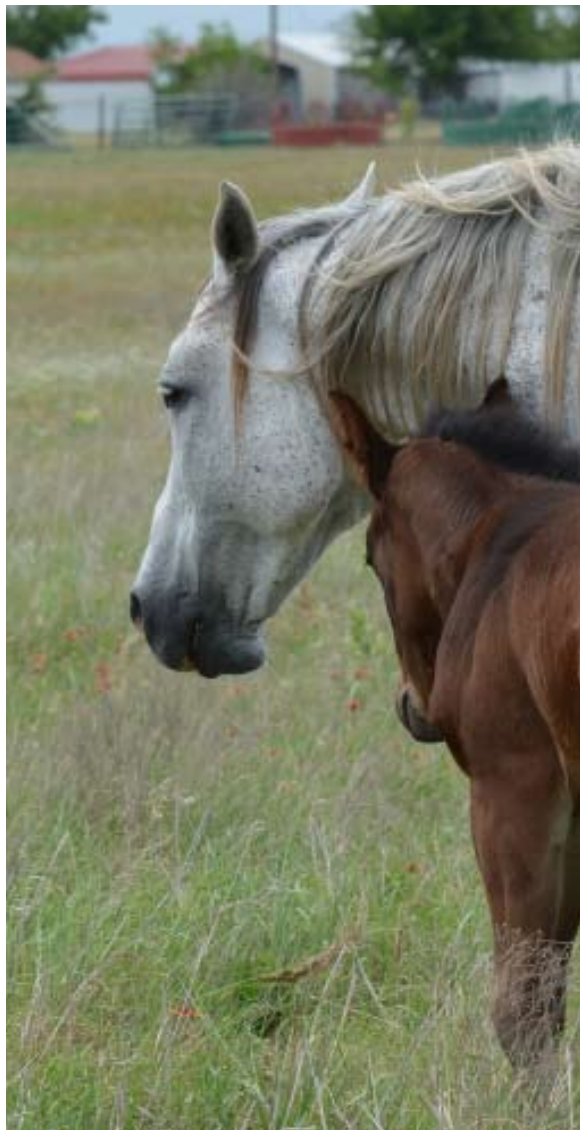
# GENETIC TESTING

*What does genetic testing mean for the stallion owner and breeder?*

By **STEVEN FISCH, DVM**



The effects of genetic diseases such as glycogen branching enzyme deficiency (GBED), hereditary equine regional dermal asthenia (HERDA), hyperkalemic periodic paralysis (HYPP), malignant hyperthermia (MH), and polysaccharide storage myopathy (PSSM) range from mild and manageable to terminal. Breeding horses in a manner that can pass these diseases on to future generations can result in added veterinary costs for diagnosis and treatment and loss of time and money spent in breeding and raising these horses. Most importantly, these diseases can cause suffering for the horses.

The American Quarter Horse Association has been proactive in researching genetic diseases in Quarter Horses, which is one reason there is so much knowledge pertaining to genetic traits in American Quarter Horses. The AQHA is now requiring all AQHA registered stallions that breed mares in 2015 to be tested for this panel of diseases. The cost is $85 per stallion for AQHA members and $125 per stallion for non-AQHA member stallion owners. While in the short term these tests increase the cost of breeding by $85 or more, in the long term, they will save owners and breeders both time and money.

The tests will also alleviate a lot of needless equine suffering. Genetic testing of stallions is a good thing for the mare owner or breeder as they make decisions on which stallion to breed their mares to, because testing lends more confidence and science to the selection process. I believe genetic testing adds to the profitability of breeding performance horses by cutting long term costs. The test is simple. The only thing necessary is a sample of your horse's mane or tail hair sent to the Veterinary Genetics Laboratory at the University of California-Davis.

The appearance of genetic diseases in our horses is due in large part to practices such as line breeding to concentrate desirable traits. While this practice does entrench the desirable traits in a line, it can also account for some undesirable traits on a recessive gene that might be in a family line. Naturally, everyone wants to breed to the most popular stallion, but the tendency for many breeders to breed to the same stallion creates a loss of genetic diversity.

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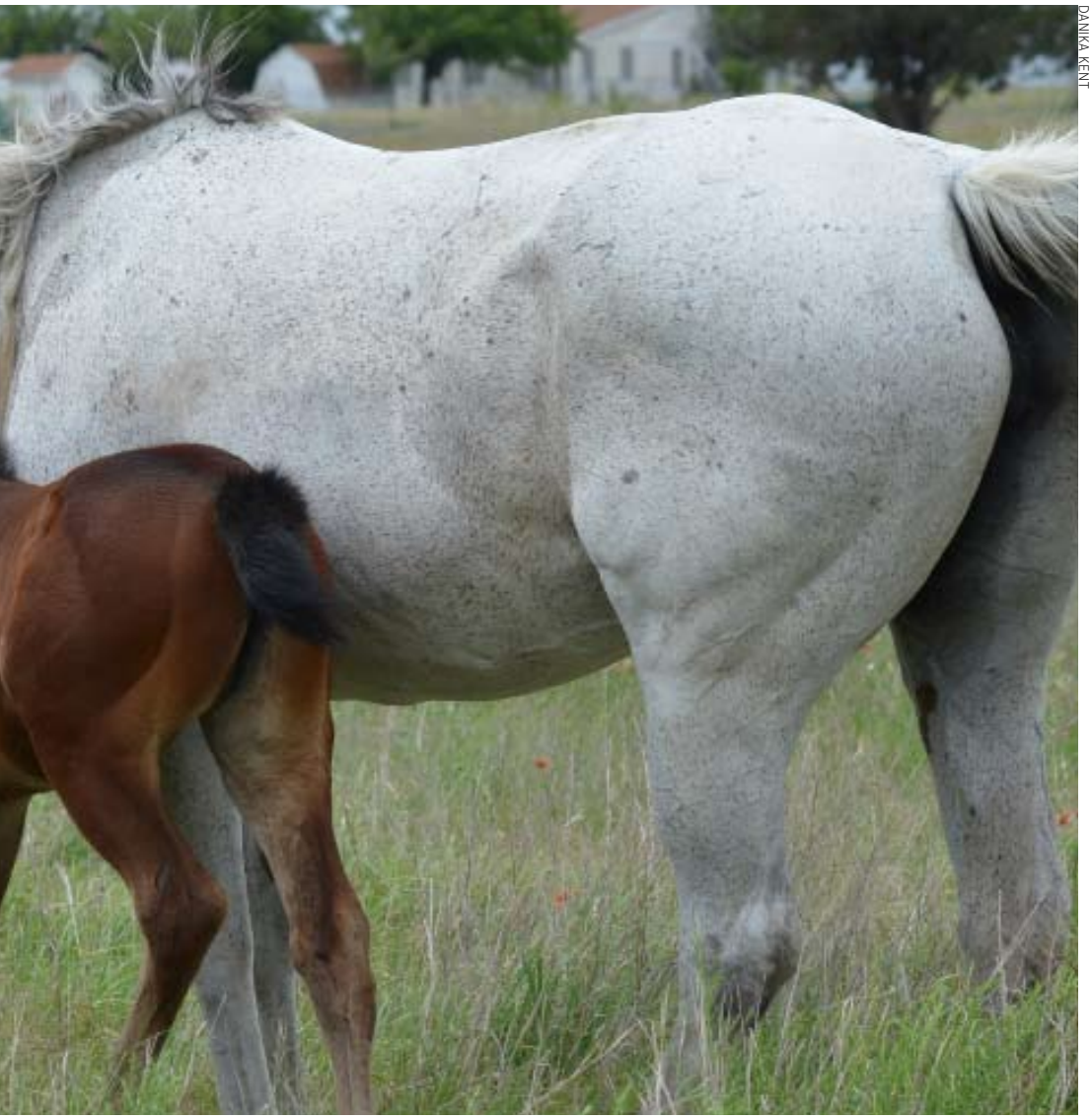
Assisted reproductive techniques such as breeding with frozen semen can also amplify one individual's influence on the gene pool. When one stallion is bred too heavily and



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his genetic influence goes beyond his death with frozen semen, it's easy to see how one stallion can influence the gene pool with an extraordinary dose of his genes. This genetic influence will include whatever detrimental recessives he may carry, if any, to be uncovered in later generations. Many of the genetic diseases being tested for were discovered after the originating stallion had either produced hundreds or thousands of foals, or after he was deceased. Early detection of these genes before breeding is critical. Identifying and testing for these genes allows the responsible breeder to breed in a manner that, while it may not rid the breed of the diseases, their incidence can be greatly decreased.

In the Quarter Horse breed overall, an 11 percent positive test rate has been found for PSSM and GBED. The incidence for HERDA in American Quarter Horses is about 3.5 percent, and the HYPP incidence is about 1.5 percent. It has been determined that the disease-causing genes were distinctly distributed within seven subgroups of performance Quarter Horses. In the halter subgroup, 56 percent of the individuals carried the genes for HYPP and 28 percent carried the genes for PSSM. The cutting, reining and working cow horse subgroups all contained the genes causing HERDA, PSSM and GBED. In the cutting subgroup, 28 percent of the individuals carried the gene for HERDA. In the Western pleasure subgroup, genes for GBED had the highest incidence, at 26 percent. HERDA, PSSM and HYPP were also present in that group. The barrel racing and racing subgroups had the lowest frequencies of the diseases tested for, with only PSSM appearing in the barrel racing and racing subgroups.

## What are these diseases, their symptoms and treatments?

Glycogen branching enzyme deficiency (GBED) doesn't allow a foal to store enough sugar in its cells for energy, and it usually dies before 2 months of age. These foals are often stillborn. The disease is caused by an autosomal recessive disease caused by mutation in the GBE1 gene. Approximately 8-10 percent of American Quarter Horses are affected by GBED, and an estimated 3 or more percent of second- and third-term abortions or stillbirths are caused by GBED.

The mutation of the GBE1 gene reduces the function of the glycogen branching enzyme so that cardiac and skeletal muscle and the liver and the brain cannot store and mobilize glycogen. Because glycogen provides energy to the muscles, the inability to properly store and mobilize it leads to muscle weakness and eventually death. Many aborted and stillborn foals whose cause of death was not previously identified might have had GBED. Foals that survive birth generally die or are euthanized within 8 weeks of age. Although a few foals have survived to the age of 4 months, sadly GBED is always fatal.

Hereditary equine regional dermal asthenia (HERDA) causes the skin on a horse's back to peel away. Early signs include the presence of weeping skin, easily tented skin that doesn't return to its initial position, sloughing skin, hematomas, wounds, and scars. The disorder is caused by an autosomal recessive disease caused by a mutation in the peptidyl-prolylisomerase B gene. Approximately 3.5 percent of American Quarter Horses are carriers. Collagen makes up connective tissues such as muscles, bones, skin and cartilage. The mutation in the PPIB gene results in defective collagen, which causes the outer layer of the skin to divide from the layer underneath. Many times, raw wounds are caused by the outer layer of skin sloughing off. Young horses with HERDA might appear to have an unusual number of cuts and nicks on their skin, but the disease

is most often noticed when the horse starts training under saddle. The pressure of the saddle on the back causes the skin to tear and separate, leaving raw areas. These areas are slow to heal, and many horses with HERDA are euthanized due to slow-healing injuries.

Hyperkalemic periodic paralysis (HYPP) is a muscle condition that leads to uncontrolled muscle twitching or profound muscle weakness. In severe cases, it can lead to collapse and death. Traced back to the stallion Impressive, HYPP was seen in his sons and daughters because to be expressed, the disease does not require two copies of the defective gene. However, successive generations of offspring that received two defective genes often show more severe versions of the disease.

The disorder is caused by an autosomal dominant disease resulting from point mutation in the SCN4A gene. It affects approximately 1.5 percent of all Quarter Horses and as many as 56 percent of all halter horses. HYPP affects both horses and humans. The genetic defect causes a disruption of the sodium ion channel, which is a tiny gateway in the membrane of muscle cells. The genetic defect disrupts the channel's normal opening and closing, such that uncontrolled sodium influxes occur. These influxes, in turn, change the voltage current of muscle cells, causing uncontrolled muscle twitching or profound muscle weakness. High levels of potassium in the blood usually are present when the disruptions in the ion channel occur. This disruption in the conduction of the nerve impulses causes muscle tremors and even temporary paralysis in affected horses.

As the following guidelines demonstrate, a horse that has HYPP demands special care, and the special care increases time and financial costs. There are certain management practices that assist in the control of HYPP. They include establishing a regular feeding and exercise schedule. Fasting and water deprivation should be avoided. Horses do better if allowed access to a paddock or pasture rather than strict stall confinement. Daily or nightly turnout helps in quenching symptoms. Adult horses do very well on grass or oat hay alone, or pasture. If it is necessary to use alfalfa to balance the ration for growing horses, then mix alfalfa with grass hay or oat hay, and grain with oats being the best grain to decrease potassium content of diet. Feed equal amounts of hay and grain two or three times daily. Rapid changes in diet should be avoided. Provide access to a white salt block or feed loose salt.

Acetazolamide is a diuretic that decreases the level of potassium in the blood. Many halter horse owners continue alfalfa hay as the only roughage in their horses' rations, but maintain their horses on this drug for all or most of their lives. Acetazolamide is a forbidden substance under AQHA and AHSA regulations. Your veterinarian should always be informed of the HYPP condition prior to any general anesthesia, which might precipitate an episode of paralysis. Maintain acetazolamide therapy before and after surgery or anesthesia.

Always err on the conservative side while hauling. Be sure to stop and water horses every two hours. If a horse shows mild symptoms, exercise the horse either by walking or lunging. Exercise stimulates adrenaline, which helps replace potassium inside cells. However, one should use caution, as the horse could stumble and fall while having muscle tremors. Feeding grain such as oats, dry corn, barley, or light Karo syrup as a glucose supplement stimulates the release of insulin and promotes potassium uptake by cells. Administering acetazolamide orally (3 mg/kg) increases potassium excretion from the kidneys and also affects glucose metabolism. For severe attacks, call your veterinarian, who may treat with fluid therapy and administration of calcium gluconate IV, dextrose 5 percent IV and insulin.

Malignant hyperthermia (MH) or malignant hyperthermia-like episodes in the horse have been associated with drugs such as halothane, isoflurane, succinylcholine,

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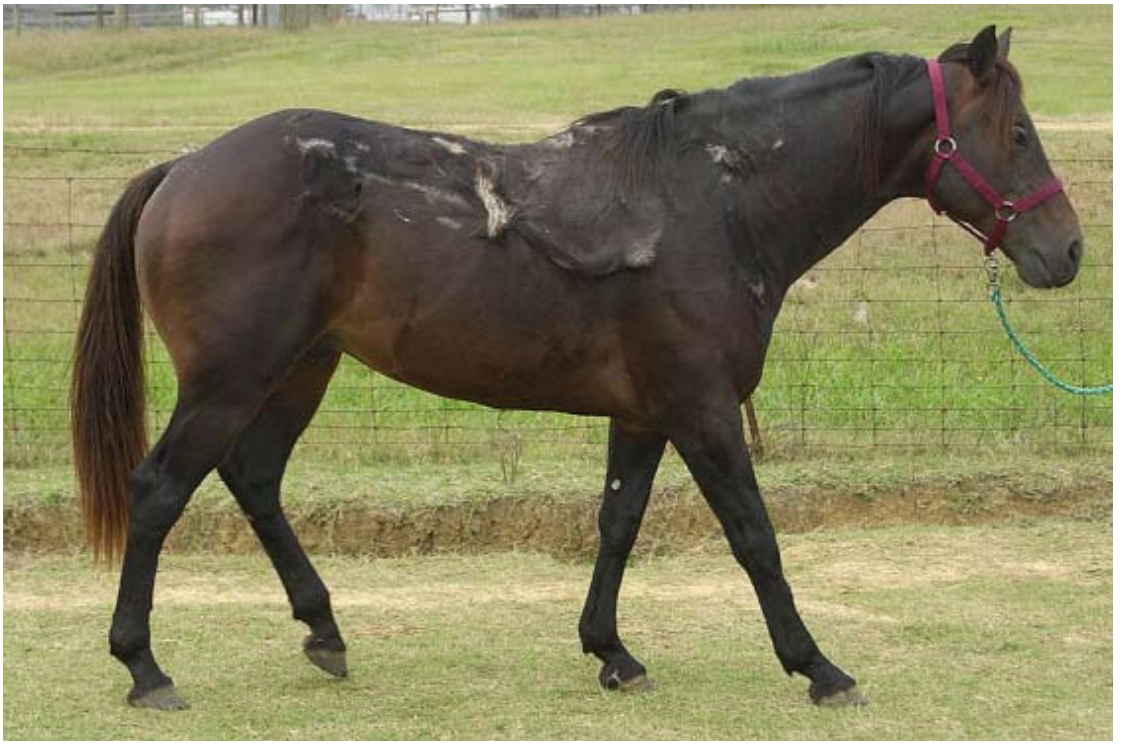
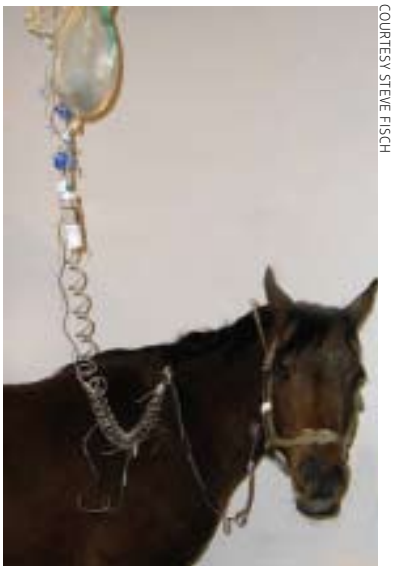


Left: Hereditary equine regional dermal asthenia (HERDA) is a genetic disease that causes the skin on the horse's back to peel away.
Below: Running fluids intravenously is among the only possible treatments for certain genetic diseases.



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caffeine, the muscle relaxant succinylcholine, and stress. Affected horses experience increased muscle metabolism, fever often exceeding 109 degrees Fahrenheit, high heart rate, excessive sweating, abnormal heart rhythm, shallow breathing, muscle rigidity, hypertension, breakdown of muscle tissue, muscle protein in the urine, and/or death. The disorder is caused by an autosomal dominant disease resulting from a mutation in the ryanodine receptor 1 (RyR1). MH affects an unknown percentage of American Quarter Horses and several other breeds. MH can make simple anesthesia deadly for some horses.

The mutation results in a malfunctioning calcium-release channel of the sarcoplasmic reticulum in skeletal muscle. The malfunction causes excessive calcium to be released into the myoplasm, which is the contractile part of a muscle cell. This can cause a great increase in metabolism and may result in death. The disorder is caused by an autosomal dominant disease caused by point mutation in the SCN4A gene. Treatment is aimed at decreasing the horse's temperature with IV fluids, anti-inflammatories and other life supporting medications. The most important treatment is prevention, hence the genetic testing for MH.

Polysaccharide storage myopathy (PSSM) is a metabolic muscle problem found in at least 20 breeds, including Paints, Appaloosas, drafts, and 11 percent of American Quarter Horses. Commonly referred to as "tying up," PSSM is an autosomal dominant disease most commonly caused by mutation in the glycogen synthase 1 (GYS1) gene. This mutation causes unregulated synthesis of glycogen, which results in excessive sugar in muscle cells.

The disorder is characterized by the accumulation of glycogen, which is a storage form of sugar and an abnormal sugar, or polysaccharide, in skeletal muscle. Affected horses develop stiffness, muscle cramping and soreness with light exercise, probably due to a deficit of energy generation in their muscles. This leads to muscle pain, sweating, exercise intolerance and weakness. Because of the stiffness and pain, horses are reluctant to move.

There are two types of PSSM. Genetic testing identified the specific mutation in GYS1 in horses diagnosed with PSSM. This is PSSM Type 1. Horses identified as having a moderate to severe form of the disease according to the muscle biopsy were more likely to have PSSM Type 1 than horses with a milder version of the disease. Type 1 PSSM is mostly seen in Quarter Horse, Paint, and Appaloosa purebreds or crosses, draft breeds, Morgans, and Tennessee Walking Horses.

Other horses did not have the mutation in the GYS1 gene, and these are the PSSM Type 2. Type 2 PSSM is found in a variety of breeds and its cause is not yet known. It is believed to have arisen from a single horse about 1,200 to 1,500 years ago.

While the physical attributes of affected horses vary widely, the extent of the muscle metabolic problem ranges from unrecognized subclinical disease to overt exertional rhabdomyolysis (tying up) to recumbency that necessitates euthanasia. Eight percent of Quarter Horses have the GYS1 mutation. Re-evaluation of horses tested by muscle biopsy and found to have the disease indicated that about 75 percent of PSSM Quarter Horses had the GYS1 mutation. A small percentage of Quarter Horses have another form of PSSM not due to the GYS1 mutation.

PSSM, or tying up syndrome, is a life-threatening condition that can be triggered by anesthesia and several other things. In horses with this gene mutation, excess calcium is released, causing clinical signs that include muscle rigidity, elevated body temperature, profuse sweating, excessively fast heartbeat, brown urine, excess carbon dioxide in the blood, muscle enzyme increases on blood tests, electrolyte disorders, rapid and shallow breathing, hypertension, acidosis or a drop in blood pH, and a high death rate.

Most PSSM horses respond well to a high-fat and low-starch diet. On a grain-inclusive diet, both diet and genotype affect clinical expression of PSSM. Horses with severe symptoms need immediate attention from a veterinarian and are usually given high volumes of IV fluids.

In summary, it appears obvious that the new AQHA rules involving genetic testing mean much less suffering for our equine friends and less cost to the stallion owner and breeder. All horse breeders should breed responsibly. Taking responsibility means taking time to be educated on these important genetic diseases to make sure we are not breeding in such a manner as to produce foals with the possibility of exhibiting these diseases and passing them on to future generations. While the temptation may be there in the short term to breed in certain patterns, in the long term, it is much too costly to do so in terms of horse health and financial and time investments. I believe that if breeders let what is best for the welfare of the horse be their guide as they choose breeding matchups, a lot of the genetic diseases will either exist at a much lower percentage, or cease to exist at all.

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## Normal or Not?

Breeding when both the mare and stallion are carriers (carry the gene but do not show clinical signs) in this example: 25 percent will be perfectly normal, 50 percent will be carriers, and 25 percent will be affected by the disease and most likely show clinical signs.

| | | Mare (carrier) | |
|---|---|---|---|
| | | I | i |
| **Stallion (carrier)** | I | II | Ii |
| | i | Ii | ii |

Breeding when the mare is normal and the stallion is a carrier, there is no chance that the foal will be clinically affected. However, 50 percent of the foals will be carriers for the genetic disorder.

| | | Mare (normal) | |
|---|---|---|---|
| | | I | I |
| **Stallion (carrier)** | I | II | II |
| | i | Ii | Ii |

*Acknowledgement to AQHA for stats and research data of each genetic disease.*

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## About Steve Fisch, DVM

Dr. Steve Fisch lives in Tallahassee, Fla., and is a 1982 graduate of the University of Georgia College of Veterinary Medicine. Dr. Fisch is one of the veterinarians at AVS Equine Hospital, which is a full-service equine hospital specializing in lameness, surgery and reproduction. Their website is www.avsequinehospital.com.