

Hyperkalemic Periodic Paralysis (HYPP)

Hyperkalemic periodic paralysis (HYPP) is an inherited disease of the muscle, which is caused by a genetic defect. In the muscle of affected horses, a point mutation exists in the sodium channel gene and is passed on to offspring. Sodium channels are "pores" in the muscle cell membrane which control contraction of the muscle fibers. When the defective sodium channel gene is present, the channel becomes "leaky" and makes the muscle overly excitable and contract involuntarily. The channel becomes "leaky" when potassium levels fluctuate in the blood. This may occur with fasting followed by consumption of a high potassium feed such as alfalfa. Hyperkalemic, which is an excessive amount of potassium in the blood, causes the muscles in the horse to contract more readily than normal. This makes the horse susceptible to sporadic episodes of muscle tremors or paralysis.

This genetic defect has been identified in descendants of the American Quarter Horse sire, Impressive. The original genetic defect causing HYPP was a natural mutation that occurred as part of the evolutionary process. The majority of such mutations, which are constantly occurring, are not compatible with survival. However, the genetic mutation causing HYPP produced a functional, yet altered, sodium ion channel. This gene mutation is not a product of inbreeding. The gene mutation causing HYPP inadvertently became widespread when breeders sought to produce horses with heavy musculature. To date, confirmed cases of HYPP have been restricted to descendants of this horse.

Symptoms and Signs of the Disease

Homozygous horses are affected more severely than heterozygous horses. Under ideal management practices, the defective gene does not appear to have adverse effects, but stress and/or increased potassium in the serum can trigger clinical signs of muscle dysfunction. Why some horses manifest severe signs of the disease and other exhibit little or no signs is unknown and currently under investigation. Unfortunately, a horse carrying the defective gene but showing minimal signs has the same chance of passing the gene to future generations, as does the affected horse with severe signs.

- HYPP is characterized by sporadic attacks of muscle tremors (shaking or trembling), weakness and/or collapse.
- Attacks can also be accompanied by loud breathing noises resulting from paralysis of the muscles of the upper airway.
- Occasionally, sudden death can occur following a severe paralytic attack, presumably from heart failure or respiratory muscle paralysis.

Attacks of HYPP can take various forms and commonly have been confused with other conditions. Because of the muscle tremors and weakness, HYPP often resembles exertional rhabdomyolysis ("tying-up" syndrome). "Tying-up" syndrome can be caused by many different circumstances, including exercising a horse beyond the capacity to which it has been trained, as well as nutritional deficiencies and metabolic diseases.

- A distinguishing feature of HYPP from "tying-up" syndrome is that horses usually appear normal following an attack of HYPP.
- Horses with "tying-up" syndrome, on the other hand, tend to have a stiff gait and painful, firm muscles of the hind limbs, rump and/or back.
- "Tying-up" syndrome is also generally associated with some type of exercise.
- HYPP, by contrast, is not usually associated with exercise, but occurs when horses are at rest, at feeding time, or following a stressful event such as transport, feed changes, or concurrent illness.

Because a horse may be down and reluctant or unable to stand during an HYPP attack, many owners have thought their horses were experiencing colic. HYPP has also been confused with seizures due to the pronounced muscle trembling and collapse. Unlike seizures and other conditions that cause fainting, horses with HYPP are conscious and aware of their surroundings during an attack and do not appear to be in pain. Respiratory conditions and choking have also been confused with HYPP because some horses make loud breathing noises during an attack.

Causes of an Attack

- Environmental factors can actually cause an attack of muscle weakness.
- Owners of HYPP-positive horses should be aware that external stimulus and events could increase the chance of paralysis onset.
 - ** Dietary changes
 - ** Fasting
 - ** General anesthesia
 - ** Concurrent illness
 - ** And exercise restriction

Prevention and Control of HYPP Attacks

Dietary management is extremely important in the management of affected horses. Dietary adjustments include:

- 1) Avoiding high potassium feeds such as alfalfa hay, brome hay, canola oil, soybean meal or oil, and sugar molasses and beet molasses, and replacing them with timothy or Bermuda grass hay, grains such as oats, corn, wheat and barley, and beet pulp
- 2) Feeding several times a day
- 3) Exercising regularly and/or being allowed frequent access to a large paddock or yard.

Due to the high water content of pasture grass, a horse is unlikely to consume large amounts of potassium in a short period of time if kept on pasture. If the horse is experiencing problems on its present diet, it is recommended to feed a diet containing between 0.6% and 1.5% total potassium concentrations.

Several drugs have been used for prevention of clinical episodes of paralysis. Horses have been treated with either acetazolamide or hydrochlorothiazide with apparent success. Breed registries have restrictions on the use of these drugs during competitions (some require a veterinary certificate).

Inform your veterinarian of the HYPP condition prior to any general anesthesia, as this may precipitate an episode of paralysis. If your horse is receiving medication, maintain him or her on therapy before and after surgery or anesthesia. Use common sense while hauling and be sure to stop and water horses frequently (every two hours).

During a severe attack of HYPP, emergency treatment from a veterinarian is necessary. For long term therapy, many horses can be managed by exercise and diet control alone. Regular exercise and access to a large paddock or pasture is preferred over stall confinement. Maintain a regular feeding schedule, preferably equally spaced, two to three times per day. Avoid rapid changes in feed, such as bringing a horse off pasture grass and immediately switching to alfalfa hay. Most horses improve when the potassium content in the diet is decreased.

Inheritance and Transmission of HYPP

HYPP is inherited as an autosomal dominant trait, which means it can occur in both males and females and only one copy of the gene is required to produce the disease. The trait is inherited from generation to generation with equal frequency; it does not get "diluted" out or skip generations. Breeding an affected heterozygous horse (N/H) to an affected heterozygous horse (N/H) will result in approximately 50% carrying the defective gene (N/H), approximately 25% will be normal (N/N) and approximately 25% will be homozygous carriers (H/H). Breeding an affected heterozygous horse (N/H) to a normal horse (N/N) will result in approximately 50% normal offspring and approximately 50% carrying the defective gene (N/H).

Expected Breeding Outcomes					
N/H x N/H have 25% chance of producing normal offspring, 50% chance of producing heterozygous carriers and 25% chance of producing homozygote offspring			N/H x N/N have 50% chance of producing normal (NN) offspring and 50% chance of producing carriers (NH).		
	N	H		N	H
N	25% NN	25% NH	N	50% NN	50% NH
H	25% NH	25% HH			

Breeding an affected homozygote (H/H) will result in all offspring carrying the defective gene regardless of the status of the other parent.

Myths about HYPP

Some people have felt that the disease can be diluted out and not carried to distant generations. This is false because an affected horse has just as much chance to pass on the trait as the affected parent which passed the gene to him. Some people also believe the horse will "grow out of it." This is not true. For unknown reasons, attacks of HYPP tend to occur most often at the beginning of intense training and fitting for shows (age three to seven years old). It is important to realize that horses with HYPP are affected for life. It is possible that older horses do not experience the same conditioning stresses as young horses or owners have discovered the best management strategies for the older horses with HYPP.

Some people also think that if a horse does not show any signs up to a certain age, it does not carry the trait. Unfortunately, this is not the case. Once again, horses with HYPP are affected for life. There was a stallion and a broodmare

with HYPP who did not show signs of the disease until age eight and 15, and both horses only experienced one isolated attack.

Owners and breeders of affected horses should inform prospective buyers of the management constraints these horses have and the potential for future episodes of HYPP.

Testing for HYPP

A DNA test is available at the Veterinary Genetics Laboratory to identify horses carrying the defective gene causing HYPP. The test detects the presence or absence of the specific genetic mutation which has been found in the extended pedigree of "Impressive" descendants. From hair samples with intact roots it can be determined whether the horse does not carry this specific mutation (a normal horse), or whether it carries one or two copies of this abnormal gene mutation (heterozygous or homozygous for HYPP, respectively).

