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**Hyperkalemic Periodic Paralysis (HYPP):
A Death Sentence or a Chance at Normalcy?**

Since information on the discovery of this gene mutation in the American Quarter Horse breed has been released, there has been no hotter topic of discussion in the equine industry. It is amazing how one single horse could have such a monumental impact on the equine industry as the sire Impressive. The good news is that even though a horse has tested positive for the HYPP gene, it does not mean the individual cannot lead a healthy productive life. With proper care HYPP episodes can be controlled or curtailed altogether.

In 1969, on a farm in Ohio, a small sorrel stud colt was born. His sire was Lucky Bar, a thoroughbred, and his dam was Glamour Bars, whose sire Lightning Bar was a half quarter horse half thoroughbred stallion by Three Bars. Three Bars was the sire of Lucky Bar making the resulting foal a 3x4 cross on Three Bars. This little colt would be named Impressive. He was bred to be a racehorse, broke to ride and sent to the track, but was so muscular he was never raced. He went on to a very distinguished show career. In 31 attempts in the halter arena he won 31 times, gained 20 grand championships and was the first World Champion Aged Stallion in the AQHA winning the title in 1974 (Steward).

Because of his superior conformation, excellent musculature, and impressive show record, he became a very sought after sire not only by quarter horse breeders but also those who bred appaloosas and paints for show at halter as well. Many of his offspring inherited their sires sensational physical qualities making them outstanding horses in the show pen. Impressive's offspring also went on to become prominent and productive broodmares and stallions. In 1992, 13 of the top 15 horses on the leading sires list were descendants of Impressive, who was himself fourth on the same list. It is estimated that more than 55,000 registered Quarter Horses, Paints, and Appaloosas around the world are descendants of Impressive (Moore).

Shortly after his first foal crop was born, owners of his foals began noticing an unusual twitching in the muscles of some of his prodigy. Because HYPP had not yet been identified as a disease in the equine – humans suffer from a genetic defect by the same name, this phenomenon was usually diagnosed as one of any number of other equine ailments. The episodes did not have a consistent etiology and varied in length and severity making diagnosis difficult. Some horses possessing the yet to be identified gene were unable to move or simply collapsed for no apparent reason (Moore).

The condition soon became a concern of the AQHA as the number of reported episodes among the quarter horse population increased and in 1989 the organization funded a project at the University of California, Davis to investigate this phenomenon. In September of 1992 the results of the UC, Davis research project were printed in the Quarter Horse Journal and the strange muscle tremors were finally given a name - Hyperkalemic Periodic Paralysis, or HYPP as it is now commonly referred to. Speculation, concern, and rumors regarding the condition proliferated prompting the AQHA to make an official statement of position. The statement acknowledged that only a small percentage, less than 1%, of the total number of horses registered by the AQHA were affected and that those affected seemed to originate from a single bloodline. It also stated that most of the affected individuals were bred for one purpose - halter competition. The statement did not name the specific bloodline at that time (Unknown 51).

In the January 1993 issue of the Quarter Horse Journal, the "AQHA Update" article reported that Dr. Sharon Spier of UC, Davis had revealed the stallions name at the December meeting of the American Association of Equine Practitioners (AAEP) while being questioned following her presentation on HYPP. Dr. Spier acknowledged that all horses found with the

disease, during her research, descended from one single quarter horse stallion - Impressive, who himself was not affected by the mutation. The furor began as many daily newspapers and every major equine magazine published articles. Unfortunately the majority of the information was elaborated upon and erroneous causing a much more detrimental effect on the American Quarter Horse breed (Unknown 51). In order to stymie the speculation and erroneous information being propagated regarding the disease, the AQHA, to their credit, began an effort to educate people about the disease by publishing informative articles in the Quarter Horse Journal.

Hyperkalemic periodic paralysis is a muscular disorder caused by an inherited genetic flaw. The genetic flaw is the result of a gene mutation that occurred during the process of evolution. Most gene mutations of this type do not propagate because the affected individual does not survive. For some unknown reason Impressive survived and the mutation was passed on to some of his offspring (Unknown 52). This particular flaw affects the cell membrane by disrupting the normal opening and closing of the sodium ion channel. These channels are "pores" in the muscle cell membrane which serve as gateways controlling the flow of sodium and potassium in and out of the cell. This flow controls the muscle fiber contraction and relaxation. In an affected horse these gateways malfunction and begin to leak, allowing potassium to flow out and sodium to flow in (Spier, Klapheke, and Cahill 18). Potassium is important for proper function of muscles and nerves and every bodily cell is comprised of potassium which plays a vital part in preserving the "charge" in the excitable muscle cells and nerves. Muscle serves as the body's "pool" for potassium and thus skeletal muscle contains the highest levels of potassium. The concentration of potassium in the blood is 25 times lower than that in cells and is controlled by various hormones including insulin, adrenaline, aldosterone, and thyroid.

Studies found that not only were affected individuals' muscle abnormal in the permeability of both sodium and potassium but that the muscle content of water and sodium were higher and

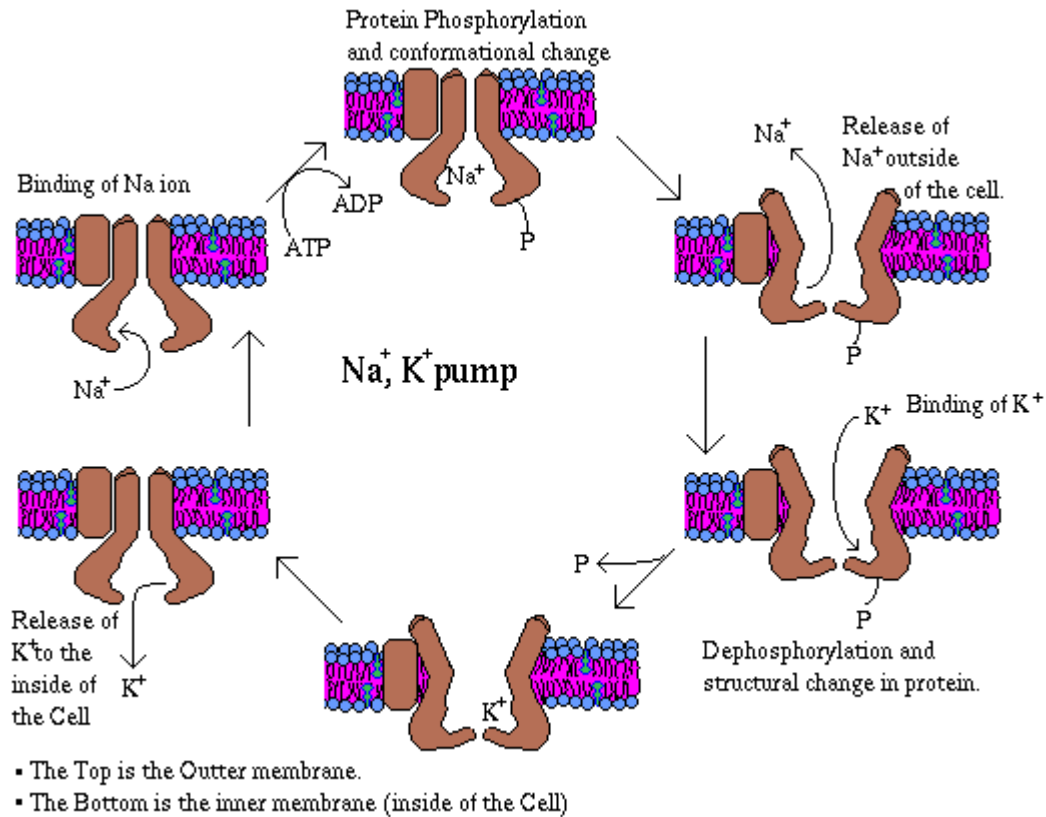


Figure 1. Na – K ATPase
(The Sodium-Potassium ATPase pump)
The Periodic Paralysis Association: An Online Biology Book

potassium lower than a normal horse. Horses, which experience an attack, have been found to have a higher level (.50 to 12.0 mEq/L) of potassium in their blood than normal (3.0 to 4.5 mEq/L) (Spier and Carlson 68). Figure 1 shows how the sodium ion channel functions.

HYPP is an autosomal dominant gene meaning that it is not sex related. Both males and females have an equal chance of inheriting the gene. Because it is a dominant gene it does not become “diluted” and is passed from one generation to the next on an equally frequent basis

(Unknown 52). The disease is not infectious or contagious - it is genetic in origin. The following table demonstrates how the gene is passed on:

Table 1
Distribution of the HYPP Gene.

	N	N		H	N
H	H/N	H/N	H	H/H	H/N
N	N/N	N/N	N	H/N	N/N

Source: Unknown 51

If a heterozygous individual (N/H), those having one copy of the gene, is bred to a normal individual, fifty percent of the offspring will be normal (N/N) while the other fifty percent heterozygous (N/H). If you were to breed two heterozygous individuals to each other, fifty percent would be heterozygous (N/H), twenty-five percent normal (N/N) and twenty-five percent homozygous (H/H), those carrying two sets of the gene. Less than 1% of the horses tested were H/H, or homozygous for the gene. There is no set pattern for inheritance - it is strictly random in nature (Groves 53).

HYPP attacks vary significantly in etiology, duration and severity. Much of it depends upon the individual. Not every horse that tests positive for the HYPP gene is symptomatic. Some horses possessing the HYPP gene go through their entire life and never experience an

attack. Heterozygous horses (N/H), are more likely to have mild or no attacks at all. Homozygotes (H/H), those horses having both copies of the gene, are more likely to experience attacks with more frequency and of a higher severity (Groves 54), though this is not scientifically proven. Usually, if a horse is going to experience an attack they will do so by the time they are five years of age but keep in mind that any individual may experience an attack regardless of age. Genetic predisposition, stresses, and diets all factor into the probability of a horse having an attack. The least understood factor is genetic predisposition, which is the inherited probability of having an attack. However, it has been determined that once an individual has suffered an attack, it is highly likely that it will experience another (Gesel 16).

HYPP can be very difficult to diagnose by simple observation because of its visual similarities to other equine diseases such as colic or "tying up." Some signs of an episode are periodic muscle spasms which look like something crawling under the skin, trembling, weakness, sweating, leaning on walls or lying down. In the case of a homozygous individual, an attack can be accompanied by noisy breathing caused by the paralysis of the throat muscle (Spier, Klapheke, and Cahill 18-19). Some horses may lose complete muscle control and collapse. Death may occur in rare cases but it is usually attributed to cardiac arrest and or respiratory failure (Unknown 52).

It is hard to factor stress into the likelihood of a horse having an attack since the types and levels stresses differ greatly. For example, in a situation where two individuals are subjected to the same living conditions and same types and levels of stresses - one might suffer an attack while the other is unaffected. Trailering might cause an episode in one individual while training or even foaling might trigger an attack in another. Hot, humid weather over long periods

of three or more continuous days seems to stress some HYPP horses and can initiate an attack. If horses are stalled provide plenty of ventilation and a fan for cooling purposes. If outside, be sure the horse has ample access to shaded areas. Always have plenty of water available for these horses. Horses are creatures of habit and like consistent routines. Every effort should be made to establish a routine for feeding and training. Try to avoid any sudden changes in routine as it could cause stress. If changes need to be made they should be done slowly over a period of time (Gesel 16-17).

A horse's physiology depends a lot upon his diet therefore, diet is very important when dealing with HYPP situations. You should avoid diets high in potassium levels (Gesel 17). Since potassium seems to be the main factor triggering an attack, by lowering the amount of potassium in the diet, the frequency of attacks can be diminished or eliminated. Most hays and sweet feeds, which contain molasses, are high in potassium content. Some individuals may need to be placed on a "complete" feed, that contains the hay and grain rations combined in a pelleted form, which in turn allows for better control of potassium levels. Other horses can still be fed hay while getting their grain source from high carbohydrate feeds such as oats, corn and barley. Still, others can be maintained on sweet feeds and hay without experiencing an episode (Spier, Klopheke and Cahill 19-20).

The 'total' dietary potassium level needs to be 1% of the total amount fed by weight. This is tricky and necessitates an understanding of the levels of potassium in common feeds. Dry grains such as corn, barley and oats are about 1/2%, and most alfalfa hay is 1.5%. Thus, if you feed equal weighted amounts, you would be at the ideal 1% level of potassium. Beet pulp is high in fiber and calories and low in potassium (.3%). This is optimal for HYPP horses though should

be supplemented with soy meal, which is higher in phosphorus, for younger horses to balance the high calcium levels in alfalfa and beet pulp. One major misconception is that HYPP horses should be fed other hays instead of alfalfa. This is misleading since many other hays contain a higher potassium level than alfalfa - timothy contains 1.8% and orchard grass 2.59% (Steward).

Besides diet and stress management, exercise plays a major role in maintaining the HYPP horse. Those affected with the HYPP gene do better with daily turnout as opposed to stall confinement. Horses experiencing an attack will benefit from light exercise such as walking or jogging, which increases the adrenaline thus lowering the amount of potassium in the blood and stabilizing the episode. As stated previously, it is thought that stress, especially in young horses, can trigger an attack (Spier, Klopheke, and Cahill 19-20). Medication plays an integral part in HYPP maintenance for some horses, especially those who suffer frequent or severe attacks. Acetazolamide is a mild diuretic that helps the liver and kidneys shed the excess potassium however it takes approximately 12 hours after being administered to become effective. Acetazolamide is now approved as a maintenance drug by the AQHA and can be used during competition however, it is still listed as a substance banned by the ASHA during competition.

It is very important to relate the HYPP status of an individual to your veterinary before any surgical procedures so that the veterinary may monitor for any signs of attack during treatment. Some tranquilizers, such as acepromazine, or those derived from phenothiazine should be avoided because they can trigger an HYPP episode by increasing the serum potassium level. Those tranquilizers acceptable for use in the HYPP positive horse include Rompun, Torbugesic, and Dormosadan.

Emergency treatments in the event of a *mild* HYPP attack include:

1. Exercise (Use caution as the horse may be uncoordinated).
2. Feed grain high in carbohydrates (corn, oats, or barley) or administer Kayro™ (light corn) syrup (approximately 50 cc at 15 minute intervals until tremors subside). You can also dissolve 2 cups of baking soda in water and administer orally. *NOTE: Do not use dark corn syrup as it contains potassium.
3. Orally administer 3 mg/kg (approximately 6 to 8 tablets) of acetazolamide which increases the potassium excretion from the kidney's and stimulates the release of insulin.

For a *severe* attack contact your veterinarian immediately. If the horse has collapsed and is unable to rise, your veterinarian should:

1. Administer 23% calcium gluconate via IV catheter. Most horses will respond to this treatment immediately and rise.
2. In the event the horse does not respond, administer interveinously 1 L 5% sodium bicarbonate.
3. If there is still no response, administer 3 L 5% dextrose interveinously, and monitor blood potassium levels.

Each of these treatments will help to lower the potassium level in the blood and also help to stabilize the muscle membranes (Spier). As a preventative you may choose to top dress feed with the light corn syrup and/or baking soda. This is often a cheaper alternative to medicating daily with acetazolamide though this may not work for every horse – some will require the medication for maintenance of the symptoms.

The AQHA continues to fund research on HYPP and, since initial reports were made, Dr. Sharon Spier, the preeminent authority on the disease, issued the following statement trying to bring the condition into perspective. "Horses afflicted with HYPP, if properly managed, can lead productive, useful lives, and bring their owners many hours of pleasure" (Unknown 51).

Anyone who owns a horse with Impressive in its bloodlines should have the horse tested if they suspect that the horse has had an attack. A DNA test developed by UC, Davis in 1992 is currently the only way to confirm the presence of the HYPP gene in an individual. The test can be performed from either a blood sample or with a strand of hair from the suspected animal.

Contrary to what many uninformed people believe, and unfortunately propagate, HYPP positive horses are maintainable and can lead very happy and prosperous lives. Many of today's top horses trace back to Impressive. Some of them possess the HYPP gene but many more do not. With proper breeding and out-crossing this genetic defect will occur less frequently and one day will possibly become obsolete. Until that day horse owners should do all in their power to become informed about this disease so that they can make knowledgeable decisions regarding the health and maintenance of their equine friends.

For additional information and first hand experience with this genetic defect and its symptoms and treatments please visit the HYPP Forum at:

<http://forums.delphiforums.com/hypp/start>

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