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THE BENEFITS OF
LASIX
FOR EXERCISE-
INDUCED
PULMONARY
HEMORRHAGE:

50 YEARS OF
SCIENCE AND
CLINICAL
EXPERIENCE

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EXERCISE-INDUCED PULMONARY HEMORRHAGE

The first record of exercise-induced pulmonary hemorrhage (EIPH) or bleeding is by the Elizabethan author and horse breeder Gervase Markham, who notes in one of his books on horsemanship in the late 1500s, in good Elizabethan English, that:

“Many hores [efpecially young hores] are often subject to this Bleeding at the Nofe, which I imagine proceedeth either from the much abundance of Blood, or that the Vein, which endeth in that Place is either broken, fretted or opened.”

Markham was describing the post-exercise presentation of blood at the nostrils, the obvious presentation of what we now know as EIPH. Horsemen had long suspected that horses also bled into their lungs during vigorous exercise,

but visualization of such internal bleeding required development of the fiberoptic endoscope.

As long ago as the early 1700s, when the foundation sires of the Thoroughbred breed were racing and breeding, EIPH was recognized as epistaxis, or bleeding from the nose. One of the most prolific sires was Bartlett's Childers, also known as Bleeding Childers for his propensity to bleed from the nose. Bartlett's Childers was unraced but distinguished himself as the great-great-grand sire of Eclipse, who is represented in the pedigree of every modern-day Thoroughbred. The flexible fiberoptic endoscope that came into use in the 1970s led to the discovery that a high percentage of exercised horses showed varying degrees of bleeding in their windpipes following strenuous exercise. What had been observed for centuries—post-race bleeding from the nose—had only been the tip of the iceberg, accounting for about 4 percent of EIPH cases.

CONTROL AND TREATMENT OF EIPH

EIPH is a hemorrhage that occurs in the lungs of animals, including horses, camels and greyhounds, and even in elite human athletes during strenuous exercise. In horses, this hemorrhage occurs in polo horses, show and event horses, barrel racing horses and any other equine athletes participating in any endeavor in which strenuous exercise is required. Airway examination suggests that almost all racehorses experience some degree of EIPH—50 percent to 95 percent with well over 90 percent of horses showing blood in their tracheas at some time in their careers.

This hemorrhage occurs when the thin membrane between the capillaries and alveolar air sacs fails due to the pressure within the pulmonary capillaries of the lung. The blood in the lungs, along with the damage from the ruptured capillaries, results in inflammation that heals with scarring, and the damaged lung tissue loses its natural ability to expand and contract. The disease is progressive and cumulative, with the scientifically demonstrated result of permanent lesions in the lungs.

In most initial cases, the hemorrhage is slight, but as more capillaries fail, the bleeding can be marked, even resulting at times in acute fatal hemorrhage. In extreme cases, the bleeding from the lungs can result in blood coming out of the nostrils as the horse runs. In this situation, the horse is in danger of faltering, thus endangering itself, its rider and the other horses and riders. In the past, before Lasix was approved for use, horses died acutely on the racetrack from EIPH. With the advent of using Lasix in horse racing, the incidence of these catastrophic events has been significantly reduced.

CAUSES OF EIPH

EIPH is caused by stress failure or the rupture of pulmonary capillaries because of the high pulmonary capillary pressures that occur during strenuous exercise. It remains one of the most researched conditions of the racehorse, and the preponderance of the scientific literature has revealed the following:

1. When EIPH is not controlled, a cycle of hemorrhage, inflammatory reaction and more hemorrhage occurs.
2. EIPH may occur at any age.
3. EIPH has not been established to be an inherited trait.
4. EIPH occurs with high frequency in both sexes.

DIAGNOSIS OF EIPH

EIPH presents in a number of ways, including the following:

Bleeding from the nose (epistaxis): Readily obvious and recognized historically, even before the inception of the Thoroughbred breed in the 1700s. May be observable in up to 4 percent of horses post-exercise.

Blood in the trachea: Readily observed by post-race endoscopic examination of the trachea. The flexible fiberoptic endoscope permits visual examination of the respiratory tract down into the major bronchi to each lung. All racetrack veterinarians carry a flexible endoscope, and this is the most common means of evaluation of both the upper airway and lungs of the horse.

Microscopic evidence of hemorrhage: Broncho alveolar lavage fluid (BAL) collection involves injecting sterile fluid into the bronchi followed by collecting this fluid to be examined microscopically. This procedure detects the subtlest form of EIPH: minimal bleeding not observable by endoscopic examination. Essentially 100 percent of horses in training test BAL positive for EIPH.

Post-mortem examination: In a small fraction of cases, horses bleed acutely into their lungs and die on the racetrack, sometimes with no obvious evidence of blood at the nostrils. EIPH has been reported as being the cause of between 50 percent and 80 percent of acute non-musculoskeletal injury-driven deaths in racehorses. Because blood may not be apparent at the nostrils, a full necropsy is required to definitively identify cases of acute death caused by EIPH.

Control is by far the best approach to EIPH, and the best method of EIPH control is pre-exercise administration of the diuretic Lasix. Administration of Lasix pre-exercise has been definitively shown to decrease the incidence and severity of EIPH. In 2009 gold standard-quality research by Australian professor Ken W. Hinchcliff and colleagues showed that Lasix decreases the incidence and severity of EIPH, findings the American College of Veterinary Internal Medicine concurred with.

No control measure for EIPH has been studied to the same extent as Lasix. Many others have been tried, including medications that enhance clotting, improve capillary stability or decrease blood clot reduction. Of those medications, most have failed to demonstrate effectiveness. Once it was discovered that Lasix helps to prevent EIPH, some horsemen began to withhold water for up to 24 hours before racing or strenuous training. There is no scientific evidence that this practice is effective, and it could be considered inhumane. Concern also remains that this practice may be used in countries where race-day Lasix is not permitted and may be a significant part of plan B approaches to EIPH in jurisdictions that choose to ban Lasix.

Once EIPH has occurred, treatment is directed at controlling the inflammation and clearing the blood and inflammatory debris from the lungs. Some veterinarians prescribe antibiotics to prevent bacterial colonization of the blood, bronchodilators to aid in removal of the blood and even hyperbaric oxygen therapy to accelerate healing. If severe enough, lung rest, such as restricting fast exercise, is required during the healing process.

WHAT IS LASIX?

Lasix is a short-acting diuretic, or “water pill,” patented in 1959 and approved for use in 1964. It is used most commonly for swelling or edema resulting from heart failure or liver or kidney disease, as well as high blood pressure. It is on the World Health Organization’s list of essential medicines as one of the most effective and safe medications needed in a health system. Tens of millions of people take this medication daily. Lasix has also been used to prevent EIPH in horses for more than 40 years, and approximately 90 percent of horses running in North America are administered this preventative medication before racing. Lasix is recommended by every major U.S. veterinary organization to protect the health and welfare of the racehorse.

The effect of Lasix when administered intravenously peaks at 30 minutes, with return of the urine to pre-Lasix concentrations within about 2 ½ hours. Lasix reduces right atrial blood pressure for up to three hours post-administration and lowers pulmonary capillary blood pressure for up to four hours post-administration. For its protective effect, Lasix must be administered on race day and no more than four hours before the race. Dehydration due to Lasix is minimal, and return to normal values occurs even before the strenuous exercise or race occurs.

THE HISTORY OF LASIX USE IN AMERICAN HORSE RACING

It has long been rumored that the then-recently FDA-approved diuretic Lasix was used to control EIPH in Northern Dancer’s victory in the 1964 Kentucky Derby. A decade later, in 1974, the use of Lasix was legalized on race day in Maryland. Two years later, a committee led by Dr. Al Gabel of the American Association of Equine Practitioners reported to the National Association of

State Racing Commissioners that Lasix “helped prevent epistaxis” and that “in many cases it restores normal performance of horses which bleed.” With strong support from the veterinary and racing community, all U.S. racing jurisdictions, except for New York, rapidly adopted a three- to four-hour pre-race Lasix rule. As the last holdout state, New York finally adopted the rule in 1995 and immediately saw a nearly 80 percent decrease in the incidence of post-race epistaxis (See chart below).

LASIX'S EFFECT ON THE ABILITY TO DETECT DRUGS

In human drug testing, diuretics present a significant concern as masking or diluting agents. This is because most drug testing in humans is performed on urine samples, and anything that dilutes the urine may well dilute prohibited substances to the point of making them undetectable. Horse racing shared this concern when Lasix use was being adopted many decades ago, but the racing industry addressed the issue by establishing the four-hour rule, whereby Lasix was administered intravenously at four hours before a race. As stated earlier, the diuretic effect abates about 2 ½ hours after administration, leaving a full 1 ½ hours before the horse goes to post. Most states now regulate that Lasix must be administered by veterinarians employed by a regulatory

authority rather than by private practitioners. In addition to the four-hour rule, drug testing in horses has moved away from urine-based testing to blood testing, which also helps since Lasix has no significant effect on the detection of substances in blood.

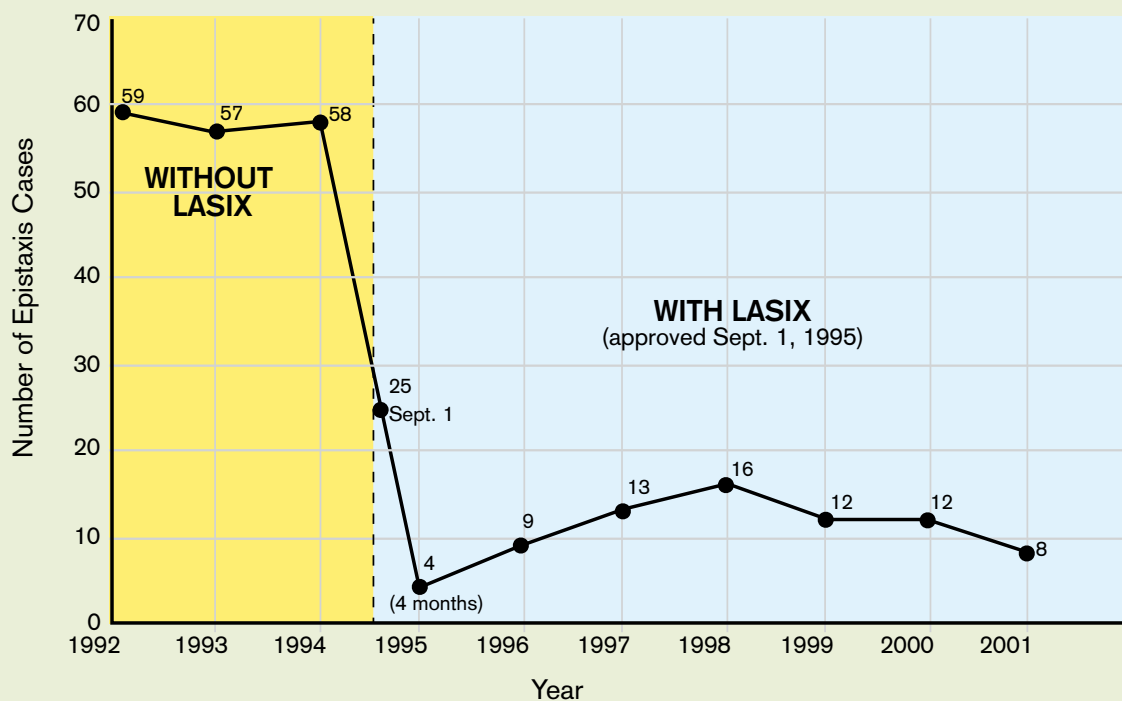
IS LASIX PERFORMANCE-ENHANCING?

Some have claimed that Lasix is performance-enhancing, so let's review a few things:

- EIPH has clearly been shown to negatively affect the performance of a horse, a fact that is not hard to understand given that blood in the lungs can dramatically interfere with a horse's ability to use oxygen.
- Numerous scientific studies have shown that Lasix decreases the severity of EIPH.
- The majority of horses performing at maximal exertion will experience EIPH at some time or another.
- It is therefore not surprising that when studies have looked specifically at the performance of horses racing with Lasix, the medication was associated with better performance.



EPISTAXIS CASES IN NEW YORK PRE- AND POST-LASIX APPROVAL



Does Lasix improve performance if there is no EIPH? Only a few studies have been designed to answer this question.

A study using tracheobronchoscopy found that male and female horses that did not bleed with or without Lasix had no performance enhancement from the administration of the medication, but geldings (castrated males) did. However, in that study, horses were raced first without Lasix, raced next with Lasix and then raced again without Lasix. Out of the 665 horses initially examined, only 79 exhibited no EIPH over the three races. Of those, only a group of 18 geldings demonstrated improved performance when Lasix was added. Curiously, in the third race, when the same geldings raced without Lasix, their form did not return to the original no-Lasix performance, indicating that the improvement in the second race was unlikely to be related to the administration of Lasix.

Another study was performed on a treadmill using oxygen consumption as a measure of performance. Because oxygen is used to generate energy, this is commonly equated to performance. This study found that Lasix made the horses lose weight and that the oxygen consumption per pound improved—but not the overall oxygen consumption per horse! Since races are run by whole horses, and not by the pound, this is further evidence that Lasix does not enhance performance, aside from its effect on reducing EIPH.

WHY DOES THE “NEW WORLD” ALLOW THE USE OF LASIX ON RACE DAY?

In countries where EIPH is often identified only through nasal bleeding, only 4 percent of actual EIPH cases are identified. Fortunately for the horse, the trainers in those countries do realize the benefits of using Lasix in training their horses. However, they are not allowed to use Lasix on race day—when the horse is going to have to give maximum effort. International markets for prospective racehorses often claim that their horses are superior because they race free of Lasix and EIPH, but despite this claim, American Thoroughbred bloodlines continue to dominate throughout the world. Further, many of the most prominent buyers of American horses are people that race outside this country. Not recognizing the proven high incidence of EIPH is one thing, but to also ignore the mounting evidence that, uncontrolled, EIPH can lead to chronic, progressive lung pathology appears hypocritical and is largely unacceptable to the trainers, veterinarians and most of the owners in North America. This statement is backed by a National Horsemen's Benevolent & Protective Association poll in which more than 90 percent of the owners and trainers were in favor of the use of Lasix on the day of the race. The North American racing industry is the largest racing industry in the world by far. To capitulate to the balance of the “Old World” is a little like the tail wagging the dog, especially in light of the substantial scientific evidence supporting the benefits of Lasix to the equine athlete.

WHY SHOULD HORSE RACING AND OTHER USES OF THE HORSE IN WHICH STRENUOUS EXERCISE IS REQUIRED REMAIN A VIABLE COMPONENT OF OUR SOCIETY?

According to the 2017 Economic Impact Study of the American Horse Council, in the United States, more than \$50 billion is directly attributable to horses, and including indirect effects, the contribution is more than \$122 billion. Direct employment in the horse industry is almost 500,000 full-time jobs, and the indirect impact contributes more than 1.7 million jobs. Green space preservation

provided by the horse industry totals 81 million acres, including 32 million acres of deeded land and 49 million acres of land leased for horse-related activities.

Therefore, despite the average American having minimal direct interaction with horses, these animals continue to significantly impact the lives of us all. Those directly involved in the horse racing industry are in awe of these magnificent athletes. Through gambling, entertainment and the sheer enjoyment of watching the most elite of athletes perform, all while preserving green space, often in metropolitan areas where such space is limited, horse racing provides all Americans with valuable benefits.

THE PROBLEM, IN OUR OPINION

Modern medicine has greatly benefited mankind. In human medicine, infant mortality has fallen by 60 percent since the time Lasix was introduced in horse racing, and human life expectancy has increased from 55 to 75 years during that time. These improvements in human health are due, in part, to modern medicine and health care.

Advances in veterinary medicine, such as the introduction of the flexible fiberoptic endoscope, have paralleled the advances in human health. Advocates for severe restrictions on medications for racehorses would have medical decisions for our cherished athletes made not by the animal's own veterinarian in consultation with the owner and trainer but by administrators in a corner office, guided by perceptions and traditions of the Old World. This would be absurd and cruel, just as it would be to deprive any animal or human of the benefits that modern medicine makes possible.

Modern therapeutic medications do not enhance performance, nor do they contribute in any way to adverse events occurring at the racetrack. Therapeutic medications improve horses' quality of life, and arguments to restrict such medications direct precious resources away from investigation of the true causes of some of our industry's problems. The medication of racehorses is more strictly regulated than medications for human athletes or for those entrusted with our safety such as airline pilots, ship captains and bus drivers. And yet some unreasonable individuals and organizations attempt to restrict medication even further. They seem to forget or do not recognize that a racehorse is an athlete.

An example of this “blame the medication” mentality is the recent response to the injuries at Santa Anita Park in California. It is disingenuous and misleading to suggest that the use of race-day Lasix was in any way associated with these injuries; in fact, if anything, Lasix decreases the likelihood of injury to both the racehorse and the jockey. Santa Anita did not have the increase in injuries in the past, and the trainers, veterinarians and apparently some other racetrack personnel were the same. If the weather was a factor, it was more likely related to how the track was maintained during the rainy weather and not the weather itself since Los Alamitos (less than 30 miles away) and Golden Gate, located in the same state and receiving about the same rainfall, did not experience similar increases in injuries.

If a stretch of highway is associated with excessive fatalities, we send out a team of engineers to determine how that stretch differs from other, safer roads. Then the road is modified in response to the investigation. This cannot guarantee that no fatalities will ever occur there, but it does return the safety to the same level as any other stretch of highway. The same type of investigation needs to be conducted every time there is any spike in severe injuries on a racetrack. The racing surface, the track base, the cushion and how it is managed in the face of weather all require careful evaluation. Such investigation should include all facets of the industry: horsemen, jockeys, racehorse veterinarians and track managers. One thing is certain—Lasix, in use for 40 years at every racetrack in California, had no role in that two-month spike in injuries at Santa Anita.

For more information on the facts concerning Lasix and EIPH, visit lasixiphfacts.com. **HJ**