9-4-2018

Lasix Lessons Learned: Science Confirms What American Horsemen Knew 50 Years Ago

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Keywords

Lasix, horse racing, performance, EIPH

Disciplines

Large or Food Animal and Equine Medicine

Notes/Citation Information

Published in *The Horsemen's Journal*, v. 65, no. 3, p. 48-50.

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SCIENCE CONFIRMS WHAT AMERICAN HORSEMEN KNEW 50 YEARS AGO

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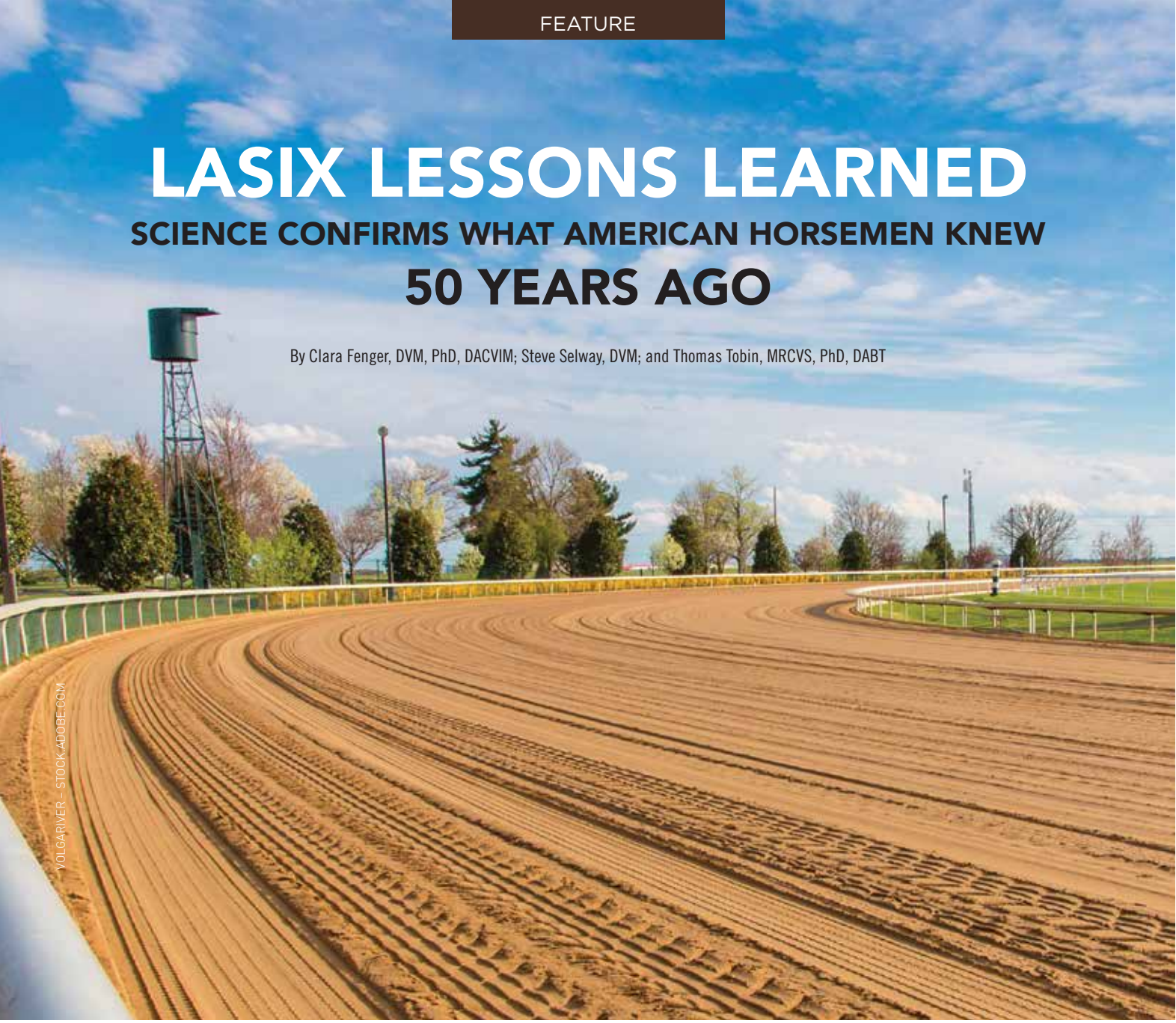

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The Lasix story is a classic American horseman's story. Bleeding from the nose in racehorses long has been identified by horsemen as performance-limiting, and nearly all modern Thoroughbreds carry the genetic code of Bartlett's Childers, a son of the Darley Arabian born in 1716. The unraced full brother of the successful racehorse Flying Childers eclipsed his brother in the breeding shed but was unable to race because he bled from the nose—so much so that he was often referred to as "Bleeding Childers." Long before anyone knew why racehorses bled from the nose, horsemen have been trying to prevent it.

The late renowned Central Kentucky equine veterinarian Alex Harthill often has been credited with the first use of Lasix in racing when he used it in another notable horse who is well represented in the genetic background of Thoroughbreds throughout the world—Northern Dancer. Harthill reportedly administered Lasix to Northern Dancer prior to the 1964 Kentucky Derby, and the legendary racehorse went on to set a Derby record that held until Secretariat broke it in 1973.

In the late 1960s, the use of Lasix became more widespread, and horsemen discovered that withholding water enhanced its protective effect. Horsemen, understanding the beneficial effects of Lasix for bleeding, lobbied for its use in American racing, and by 1995, New York, the last holdout, had approved Lasix for use in racing.

Reviewing Lasix in horse racing in 1976 for the National Association of State Racing Commissioners, Dr. Al Gabel and his colleagues noted that Lasix "helps prevent epistaxis" and that "in many cases it restores normal performance of horses which bleed."

The bottom line is that almost half a century ago American horsemen confidently had identified the protective effects of Lasix against pulmonary bleeding in racehorses. Horsemen's insights and scientific progress have slowly been confirming this ever since.

Soon after Gabel wrote his review, the fiber-optic endoscope became available. The endoscope allowed veterinarians to look into the trachea of horses post-race, confirming horsemen's long-held suspicions. Racing horses did indeed bleed into their lungs during racing, so-called occult bleeding, which accounts for unexpectedly poor performances that Lasix protected against. Another outcome was that pulmonary bleeding in racehorses got a new and more sophisticated scientific name, exercise-induced pulmonary hemorrhage (EIPH).

An early concern about Lasix was its potential effect on the detection of drugs in urine. As a diuretic, Lasix produces a transiently dilute urine, with the issue being that the resultant dilution of many drug types and especially drug metabolites could be present in the sample. This led to regulatory concerns that the use of Lasix would permit the illicit use of drugs that could escape detection.

The industry rapidly addressed this issue. The dilution effect of Lasix was shown to be primarily in effect for the first two and a half hours after its intravenous administration, and a number of subsequent studies by research groups in Kentucky under Dr. Thomas Tobin and in Pennsylvania under Dr. Lawrence Soma confirmed that three hours after Lasix administration, the dilution effect is largely over. Therefore, as proposed by the American Association of Equine Practitioners, the four-hour Lasix rule was validated in the early 1980s in a study coordinated by Drs. George Maylin and Rick Sams, clearing the way for the approval of Lasix in American racing. At four hours post-administration, the intravenous administration of Lasix was determined to not significantly interfere with the detection of drugs in urine. This approach was later considerably reinforced by inclusion of a 1.010 urinary specific gravity requirement in the Lasix rule.

By the late 1980s, the legal use of Lasix under strict regulatory guidelines was in place in most U.S. jurisdictions. Soma and his research group in Pennsylvania had previously established that Lasix improved performance in documented "bleeders," but no evidence had yet been provided about the performance effect of Lasix on the small percentage of horses that did not experience EIPH. The Pennsylvania group then tried to fill that void by evaluating the effect of Lasix on racing performance in the absence of EIPH by including endoscopy in the research design.

In 1990, Dr. Corinne Raphel Sweeney and colleagues reported on this study, in which they performed endoscopies on horses that raced first without Lasix, a second time with Lasix and a third time without Lasix. The research group found no effect of Lasix on racing performance among colts and fillies in the absence of EIPH, although they found an effect in geldings. Interestingly, the improvement in the performance of geldings was observed from the first, no-Lasix race to the second Lasix race, but the geldings did not revert to their previous form when returning to no Lasix in the third race. Therefore, the change in performance in geldings in that study cannot be solely attributed to the addition of Lasix. It can be argued that higher numbers may have demonstrated a performance-enhancing effect on the fillies and colts as well or, alternatively, may have clearly demonstrated that Lasix has no performance-enhancing effect at all, outside its ability to normalize performance by mitigating the severity of EIPH.

In an attempt to address whether Lasix enhances performance above its ability to normalize the performance of an EIPH sufferer, Dr. Warwick Bayly and colleagues at Washington State University studied five research horses on a treadmill with the results presented at the 2017 American Association of Equine Practitioners Convention. The key performance marker in their landmark study was oxygen consumption. For the exercise physiologist, oxygen consumption is used as a measure of the amount of aerobic work performed by the animal. As a rule, the more elite an athlete, the higher its oxygen consumption. Bayly and colleagues showed that horses lost, on average, 14 more kilograms (30.9 pounds) when administered Lasix. They also found that the weight-adjusted oxygen consumption improved with the administration of Lasix. In other words, each kilogram of the horse was able to use more energy and oxygen, but the entire, lighter horse ran the same distance at the same speed. While commonly quoted as support that Lasix is inherently performance-enhancing independent of its effect on EIPH, this paper is actually strong evidence to the contrary.

The approval of Lasix in New York racing in 1995 further supports the benefit of Lasix in that it "helps prevent epistaxis." New York had long kept records on the incidence of epistaxis, or frank bleeding from the nostrils, during or after the race. Review of these figures in 2000 showed that the 1995 approval of Lasix in New York racing reduced the incidence of epistaxis by a "greater than 400 percent decrease," according to Dr. Anthony Verderosa, the New York Racing Association chief examining veterinarian.

Around the same time, a major study by Diane Gross, Paul Morley and colleagues looked for an association between Lasix administration and racing performance. They analyzed the racing times for all Thoroughbreds that finished a race on dirt in the U.S. and Canada between June 28 and July 13, 1997—a modest 22,569 in total. Overall, 74 percent of these horses ran on Lasix, and the horses on Lasix raced faster, earned more money and were more likely to finish in the top three positions. The authors concluded that Lasix use is apparently "associated" with superior performance in Thoroughbred racehorses. Given the number of horses and the quality of the statistical analysis, it's a compelling study. Of course, the horses were not evaluated endoscopically, so the study cannot determine whether the horses had performance enhancement by Lasix or simply whether their performance was normalized by the mitigation of EIPH.

The authors of this study were careful to use the word "associated," which also was used by another major study in this arena. In 2005 Dr. Kenneth Hinchcliff and co-authors reported a study on the relationship between EIPH score and performance in 744 Thoroughbreds running in Melbourne, Australia. The results of this study showed that horses with EIPH scores of 1 or less were four times as likely to win and three times as likely to be in the 90th percentile for higher race earnings than were horses with grade 2 or greater EIPH. The authors concluded that EIPH is "associated" with impaired racing performance in horses racing in Melbourne. Since no Lasix was used in any of these races, the picture gradually comes into focus.

The critical study that definitively answered the question of whether Lasix administration influences the incidence of EIPH was also conducted by Hinchcliff and colleagues. The experimental study was performed in 2007 in South Africa and involved 167 horses in what is called a cross-over study. Half of the horses received saline and the other half received a full clinical dose of Lasix,

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500 mg IV. Then, seven days later, the study was repeated, with the treatments "crossed-over," i.e., the horses that had received Lasix now received saline and the horses that had received saline now received Lasix. This exquisite design allows each horse to serve as its own control, showing how each horse and its own EIPH severity responded to the administration of Lasix. The outcome of this study, published in 2009, was clear: Horses receiving Lasix had a decreased incidence and severity of EIPH, fully supporting the almost half-century-old opinion of American horsemen.

In 2014 another study was conducted in South Africa on the effects of EIPH on the racing performance of 1,000 Thoroughbreds, with results similar to the 2005 Australian study. The conclusion was that the "findings provide strong corroboration of previous research indicating that the occurrence of EIPH has a major impact on the ability of Thoroughbred racehorses to compete successfully as elite athletes."

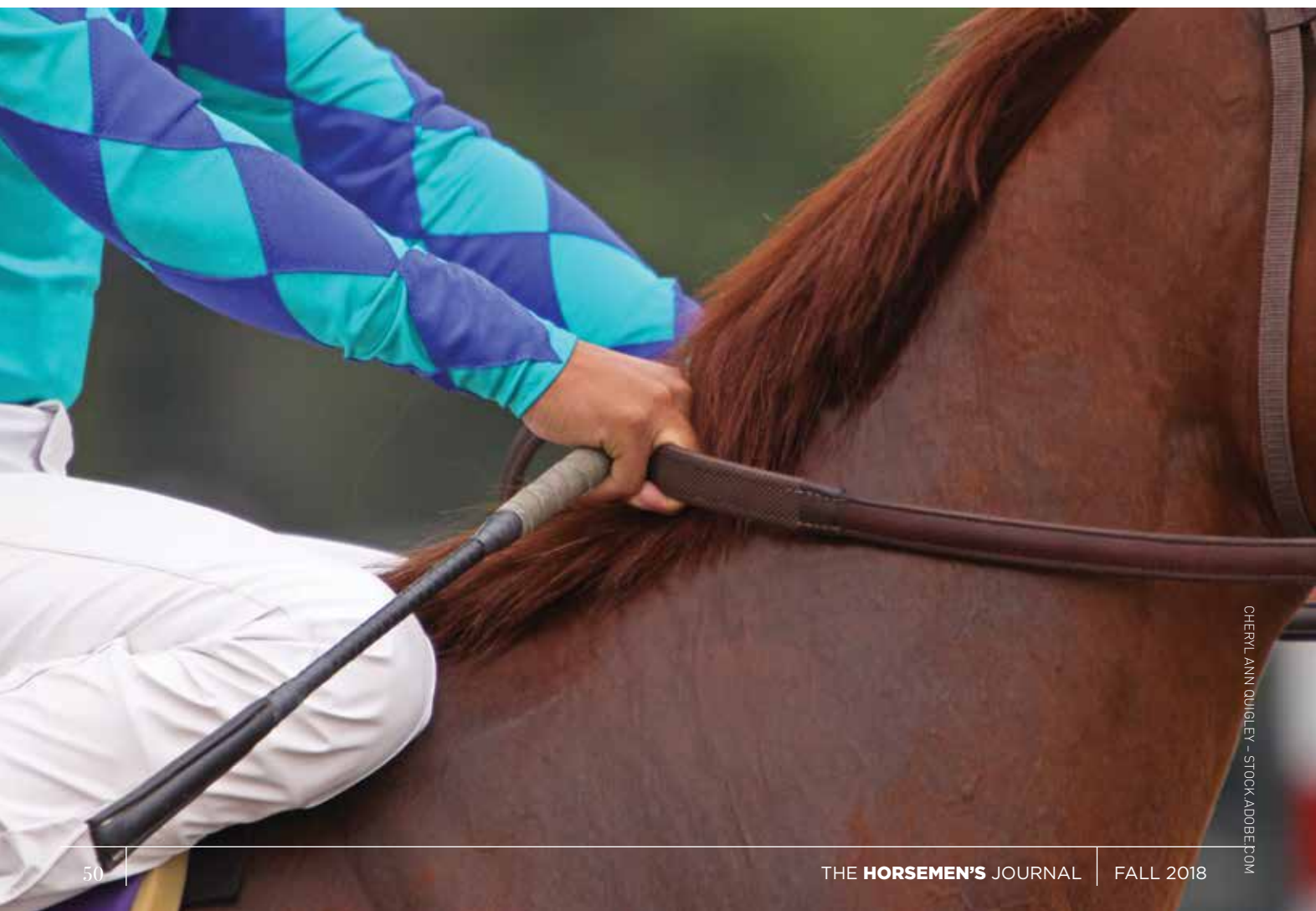
Note that the authors said "major impact."

So, long story short, horsemen in the 1960s correctly identified Lasix as effectively protecting racing horses against EIPH and its adverse effects on racing performance. Their belief in this clinical judgment led to Lasix being approved throughout the Americas and most particularly in North America. This, in turn, led (eventually) to rigorous scientific evaluation of the actions of Lasix on EIPH and racing performance. These studies fully supported the long-standing clinical opinions and experience of American horsemen with respect to EIPH, its effects on horses and racing performance and the protective effect of Lasix, as noted by Gabel and his colleagues in 1976.

One last question is "Why were American horsemen so far ahead of the scientific community?" The answer is simple: Successful horsemen and their veterinarians make far more intuitive, precise and astute evaluations of the horses with whom they share their lives as compared to most scientists.

The basic standard of proof in science is a 95 percent probability that the result is correct, while identifying a horse to win the Kentucky Derby, one of 20,000 or so horses foaled in a year, is a far more discriminating judgment. Basically, horsemen applied their solid practical knowledge and experience and correctly assessed the protective effects of Lasix on EIPH. Additionally, there are at least 30,000 horsemen running horses, and all it took was one to make the initial Lasix-EIPH connection and it took off from there. All of the early scientific evaluations, however, were with relatively small numbers of horses, some on treadmills, and these experiments gave conflicting results at best. It was not until Hinchcliff and Morley and Gross began to evaluate serious numbers of horses (700 to 1,000) and 20,000-plus racing times that their rigorous, large-number evaluations confirmed what horsemen had known all along about water withholding, Lasix and what came to be known as EIPH.

In closing, since the introduction of Lasix in the 1960s, horse racing has made substantial progress in understanding EIPH and protecting horses against the adverse effects of bleeding. In the late 1970s, availability of the fiber-optic endoscope allowed identification of the so-called "occult bleeder," or blood in the trachea post-race, and the syndrome was named EIPH and a useful scoring system was developed. Since then, EIPH has been recognized as a progressive disease in racehorses, and moderate to severe EIPH is associated with reduced racing performance. Then in 2009, scientists, using 167 horses, provided high-quality evidence that Lasix is effective in the prevention of EIPH and, consistent with this finding, that Lasix administration is associated with more reliable and optimal performance in Thoroughbred racehorses. **HJ**



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