

The fight for air

Medication may not be the answer to stop exercise-induced pulmonary hemorrhage

By Robin Stanback

Research has shown that more than half of all racehorses have some degree of exercise-induced pulmonary hemorrhage (EIPH). Some experts say that almost every high-performance equine athlete experiences some form of bleeding in the lungs. The key word is degree. For many horses, a small amount of blood leaking into the lungs is absorbed with little to no adverse effect on the individual or its performance. For others, the story is quite different.

Horses that are severely affected by EIPH may not be able to perform at all on the racetrack. However, in many racing venues in the United States and Canada, furosemide (Salix) is believed to offer enough relief to enable these horses to race.

At least one drug new to equine therapy has been approved for use in conjunction with Salix. Researchers debate the efficacy of both.

EIPH and furosemide

For a century or more, people believed that strenuously exercised horses that bled during or after exercise were bleeding from the nose. In 1970 W. Robert Cook, F.R.C.V.S., Ph.D., (now professor of surgery emeritus at Tufts University school of veterinary medicine) suggested that epistaxis, the scientific term for bleeding from the nose, originated from the lungs. It was not until John Pascoe, B.V.Sc., Ph.D., now the executive associate dean of the school of veterinary medicine at the University of California at Davis, used a fiber optic bronchoscope to examine these horses that the blood was determined without question to be originating in the lungs.

Research showed that during exercise, horses have unusually high blood pressure in the vessels that lead from the heart to the lungs, and it is believed that this high blood pressure in the small vessels could cause them to break and bleed into the airways.

Kenneth Hinchcliff, B.V.Sc., Ph.D., was the lead author of a report on EIPH completed at the University of Melbourne in 2005. In that

study, the researchers found that 55% of the 744 horses examined after racing had developed EIPH to some degree. The horses were given an EIPH grade of one to four. Horses graded a one or lower were determined to be more likely to win a race or come in second or third as were horses without a trace of blood in their airways. However, the odds of finishing in the top three places were markedly worse for horses with EIPH of grade two or higher.

“We could actually quantify the distance EIPH would affect the horse based on the severity of the disorder,” Hinchcliff said. “If a horse was a grade-three or grade-four bleeder, it was one to six meters (about three to nineteen feet) behind in race distance.”

Furosemide, a diuretic drug marketed as Lasix for use in humans to treat high blood pressure, was approved in the 1970s for equine use to treat horses with EIPH (the name was changed to Salix in 2000), although most research studies have not shown that the drug offers a definitive benefit to the horse. Salix can dehydrate a horse that is getting ready to race. This dilutes the urine and makes it difficult to detect illegal drugs.

“Actually, the horse is likely to perform better because it has lost weight,” said Eric Birks, D.V.M., Ph.D., assistant professor of exercise physiology and sports medicine at the University of Pennsylvania’s New Bolton Center. “Salix is a diuretic. Horses given Salix lose weight. Yes, they do have a decrease in blood pressure within the circulation of the lungs, but it is not a therapeutic change.

“It is rather like stock car racing. If you shave off a couple of pounds from a stock car and keep the same engine in it, it will go faster,” he said. “Salix may improve performance in the same fashion, but it is not because it has a positive effect on EIPH.”

Adjunct bleeder medications

Aminocaproic acid (Amicar), like Salix, is a medication first approved for use in humans, primarily to curb bleeding after surgery. Amicar

is a fibrinolysis inhibitor- it is designed to inhibit the breakdown of blood clots. In early equine studies of the drug conducted at Oregon State University, researchers found that Amicar enhanced clot maintenance and stability. While this research indicated that Amicar might help some equine patients, it did not assess the drug's effects on EIPH.

"Most studies indicate that the bleeding of EIPH is stopped not by clots but rather by resealing of vascular endothelium (the lining of blood vessels)," Birks said.

Horsemen still hoped that when used in conjunction with Salix, Amicar might be able to help extend horses' racing careers.

Birks has a manuscript now before a juried audience that may put an end to that hope.

"Controlled studies have been done at the racetrack," he said. "Preliminary data suggest that Amicar does not limit EIPH, even when added to Salix."

"We've seen that horses working at peak performance can be affected by EIPH," said Howard H. Erickson, D.V.M., Ph.D., professor of physiology at Kansas State University. "Researchers have also identified a smaller degree of bleeding into the lungs of racing greyhounds, racing camels, and horses working submaximally. It is a serious problem. However, some of the medications and alternative therapies currently being used may help to prevent the problem."

Erickson and his colleagues were granted research money by the American Association of Equine Practitioners Foundation Inc., the Grayson-Jockey Club Research Foundation, and the Racing Medication and Testing Consortium to study the effects of Amicar and conjugated estrogens on horses.

"Preliminary results with both treatments indicate a trend toward less EIPH, a decrease of about 50% in the amount of hemorrhage," Erickson said. "Amicar is a clotting agent. It could have unanticipated consequences, such as colonic clotting or clotting in a limb."

Erickson and his associates and colleagues around the world who focus on EIPH have studied several different medications and alternative methods to help alleviate the severe symptoms of EIPH. Among some of the

treatments used were a concentrated equine serum manufactured from draft horses. It is not used extensively, but field studies indicate some efficacy for chronic bleeders. These results are supported by treadmill studies in the laboratory.

The product traditionally has been given in a series of five injections, 24 hours apart, with weekly boosters thereafter during training and performance for five or six weeks. Whether horses treated in this fashion can return to peak performance has yet to be determined.

Another attempt to alleviate the symptoms of EIPH was the use of nitric oxide to lower the blood pressure in the blood vessels in the lungs.

"Nitric oxide did not prove to be helpful; there was actually more bleeding in the lungs," Erickson said. "It made symptoms worse, possibly by relaxing the little sphincters ahead of the very small blood vessels in the lungs. Herbal remedies have also been used, but there is no evidence that they are effective in reducing EIPH. However, a diet supplemented with omega-3 fatty acids may be effective by reducing airway inflammation and pulmonary vascular dynamics. Nasal strips seem to be a different story."

In 1993, Breathe Right nasal strips were introduced to the human market to provide drug-free relief from problems such as snoring, nasal congestions, and the temporary relief of breathing difficulties due to deviated septum. Professional athletes began using the strips, saying they helped enhance their performances.

Because horses are obligate nasal breathers- unable to breathe through their mouths- they experience some level of nasal-tissue collapse during heavy exercise. This results in a reduction of the size of the airway, causing the horse to work harder to get the oxygen it needs.

In 1999, Jim Chiapetta, D.V.M., and Ed Black, D.V.M., M.S., took that knowledge and decided to modify the strips used for humans to accommodate the horse's larger nasal passages. The strips developed were drug-free, self-adhesive, and disposable.

"They were designed to be placed over the part of the nasal passages not supported by bone," Erickson said. "The thinking was that they would mechanically support the nasal

passages of the horse during heavy exercise and reduce airway resistance. We were asked to evaluate them and found that they did reduce bleeding in heavily exercised horses, primarily the severe bleeders. These results have been confirmed by studies in other laboratories and on the racetrack.”

Sandra C. Valdez, D.V.M., was the lead researcher for a 2004 clinical study at the University of California at Davis to determine the effects of a nasal strip on the presence of red blood cells in fluid washed from the lungs after exercise of racing Thoroughbreds at Golden Gate Fields. Her results indicated that the use of the strips might decrease pulmonary bleeding, particularly in horses with severe EIPH.

The great debate

Conflicting research results are nothing new to the Thoroughbred racing industry. Studies on horses affected by EIPH cover a wide gamut from nasal strips to Chinese herbal medicines. Almost all can refer to some form of research or anecdotal evidence to advocate their use. Many reports answer one question, only to open the door to others. Because nasal strips hold open the nasal passages, will the horse inhale more dust from the racetrack surfaces? Will that additional dust have an adverse effect on the horse’s respiration? What if the horse is running on a synthetic track?

“Researchers have been studying EIPH since 1981,” Birks said. “We’ve looked at the heart, lungs, blood pressure, and the effect medications have upon the horse’s systems. To date, there does not appear to be any specific solution.

“We think that lowering the blood pressure in the lungs significantly, more than can be achieved, with the use of furosemide, might help to stop EIPH. The next step would be to study that effect on performance. Do the horses run as well if we significantly lower the blood pressure?”

“The only certain method of helping a horse with EIPH may be rest,” Erickson said. “The problem is that racing is a financial process. People want to bring their horses back to racing as quickly as possible. There are built-in restrictions in most racing venues that help to protect the horses. If a horse bleeds once, it is

given a mandatory period of rest. If it bleeds twice, it is rested for an even longer amount of time.”

For now, rest remains the best way to help a horse recover from bleeding during and after exercise. Researchers continue to study the mechanisms of EIPH and to explore new avenues of treatment. Even though much has been learned, there are still more questions than answers.