



EXERCISE INDUCED PULMONARY HEMORRHAGE

By Dr. Larry Bramlage - Summary results of a pair of research projects

Two research projects on Exercise Induced Pulmonary Hemorrhage (EIPH) solicited by The Grayson-Jockey Club Research Foundation and funded in cooperation with The Jockey Club, the AAEP Foundation, Keeneland Association, Oak Tree Racing Association, The Stronach Group, Churchill Downs, Kentucky Downs, New York Racing Association, The Del Mar Thoroughbred Club, Oaklawn Park, and The Thoroughbred Horseman's Association have now appeared in peer-reviewed journals.

Knuch H K, Wilson WD, Vale A, et al. Effectiveness of furosemide in attenuating exercise-induced pulmonary hemorrhage in horses when administered 4- and 24-hours prior to high speed training. *Equine Vet J.* 2017;50:350-355.

Bayly W, Lopez C, Sides R, et al. Effect of different protocols on mitigation of exercise induced pulmonary hemorrhage in horses when administered 24 hours before strenuous exercise. *J Vet Intern Med.* 2019;1-8. <https://doi.org/10.1111/jvim.15574>

In March of 2015, a special call for research on exercise induced pulmonary hemorrhage was issued by the Grayson-Jockey Club Research Foundation. Emphasis was placed on strategies to control EIPH without race-day medication. Two projects were selected. **The premise of the research was to look at the post-treatment effect of furosemide (Salix, or Lasix) if it had been given 24 hours before exercise with water intake limited to maintenance water levels (which are known).**

One project submitted by the University of California at Davis under the direction of Dr. Heather Knuch proposed to take 15 fit Thoroughbreds with no known history of bleeding and assess three treatments head-to-head against each other: saline placebo, furosemide four hours before exercise, and furosemide 24 hours before exercise with limited water access. The horses were paired in five-furlong simulated exercise sessions and assessed for bleeding via endoscopic examination using the conventional 0-4 scoring system and via broncho alveolar lavage (BAL) counting the number of red blood cells (RBC) found in the lung lavage post exercise. The horses trained conventionally at a racetrack, and the exercise sessions were separated by a two-week interval.

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The results showed with 24-hour administration the pharmacologic level of furosemide is approximately 1/100th the level of circulating medication when compared to four-hour pre-exercise administration. So, more than 99% of the medication has cleared by 24 hours.

In the horses with no known bleeding history, there was one bleeder. He bled with no treatment, and he bled through both treatments, though the four-hour furosemide treatment reduced his grade of bleeding. There were three endoscopic graders and blood in the trachea was seen in 11 of the 43 endoscopic exams; on four exams was the blood more than a grade 1 (trace) and three of those four observations were accounted for by the one horse that bled continuously.



On average there were low levels of RBC's present in the BAL in all horses after exercise, even with no blood visible endoscopically, but the levels were less than 200(105/ml), even with the bleeding horse included.

So the conclusion from the study was that, though blood was seen on the endoscopic exam of 11 of 43 endoscopic exams, the four-hour furosemide reduced the number of times blood was observed compared to the 24-hour treatment, and the BAL

results suggest the 24-hour treatment is not as effective as the four-hour treatment in attenuating the increase in RBC's associated with exercise in these horses with no known history of bleeding.

The second project done at Washington State University under the direction of Dr. Warwick Bayly took seven fit Thoroughbreds that were known to be clinical EIPH patients during racing and look at seven different treatment protocols.

The target was to assess the efficacy of furosemide at the maximum and minimum dosage administered 24 hours prior to exercise compared to the conventional four-hour treatment prior to exercise. This required seven different maximum exercise sessions from all seven of the horses separated by two weeks of routine training. The seven treatment protocols were designed to separate all the effects of furosemide and the timing of its administration to pinpoint the differences in effect of each treatment component.

The study was a two-phase project: The first segment was to look at the components of treatment with horses performing only on a treadmill, where exercise could be controlled and the horses taken beyond their aerobic capacity (115% of VO₂ Max) and exercised to fatigue where they could no longer maintain



a constant speed of exercise. Each of the horses was examined with the conventional endoscopic examination and with BAL RBC assessment post-exercise. But since the horses were known "bleeders," the BAL counts compared differences in BAL numbers two days

before exercise and BAL numbers post-exercise in addition to absolute RBC numbers to pinpoint further the effect of the treatment protocols on the "bleeding" occurring in these horses. Then with the results of these trials the horses were returned to the racetrack, trained for an additional month conventionally, and ran a simulated five-furlong race from the

starting gate with all horses receiving the most promising treatment selected by the treadmill trial data and competing against each other in the races.

All seven horses underwent the seven components of the study in a double-blinded, randomized fashion: placebo (saline), conventional (low dose, 250mg, 5ml) furosemide four hours pre-exercise, controlled water access only with no medication (maintenance water access for 24 hours pre-exercise), low dose furosemide (250mg, 5ml) 24 hours pre-exercise with free access to water, high dose furosemide (500mg, 10ml) 24 hours pre-exercise with free access to water, low-dose furosemide with maintenance water access, and high-dose furosemide with maintenance water access.

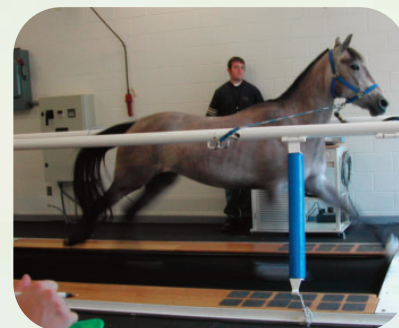
In the study of horses that were known bleeders (Washington State), the findings were as follows: No treatment produced a statistically significant difference in the endoscopic bleeding score on the treadmill because all horses bled, and the differences on the 0-4 bleeding scale were not enough to show significant changes.

However, in the BAL's assessment, where the counting range was much larger and more sensitive, the low dose (250mg) furosemide with 24-hour maintenance water was the only treatment that statistically significantly reduced the increase in the number of RBC's in the BAL fluid after exercise.

So, it was the treatment that was selected for validation in the simulated races of the six horses, one race with low-dose furosemide and one race with the saline control. The horses were fit after the treadmill exercise, but they were trained an additional month on the racetrack before the simulated race. The races were among six horses going 1,100 meters (5 1/2 furlongs) from the starting gate and were separated by two weeks of training between.



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The results after simulated racing produced some interesting changes in results. The difference between the BAL RBC's in the control horses and the treated horses narrowed, dropping the confidence of a treatment effect to 90% from 95%. This is below the traditional 95% significance threshold reached on the treadmill study but is still 90% certainty the low-dose furosemide with controlled water access lowered the BAL RBC's during the simulated races. But, the endoscopic EIPH scores on the racetrack actually changed in the opposite direction; i.e., the bleeding was worse, and the endoscopic bleeding scores became statistically significantly lower with the low-dose furosemide, water-restricted horses when compared to the control exercise values.



In conclusion, it looks like low-dose 24-hour furosemide with controlled water access shows great promise as a replacement treatment for our conventional four-hour pre-race treatment for EIPH in horses that are bleeding. It was less effective in horses that were not known bleeders.

Turning Research Into Action The Comeback Kid

By Kathryn Stemme, Owner

Diva has not had an easy life. After being purchased for top dollar as a yearling and winning several Western Pleasure futurities as a 3-year-old, the double Zippo Pine Bar mare found herself caught in the crossfire of a falling out between trainer and owner. She ended up spending several years in a field with a gelding and a herd of cows for company, until one day my sister, mom, and I heard about her story and went to investigate her as a potential project horse, due to my sister's old show horse's needing to be retired.

After months of re-training, rehabilitating, and mentally rehabbing Diva, we finally got her to come out of her anxious shell. Her kind personality and stunning markings quickly made her one of the barn favorites.

One 4th of July after getting Diva, my sister and I were headed to an open show to sharpen up our showing skills. We loaded up our horses, including Diva, and headed to the fairgrounds about 10 minutes away from our house.



Diva after her first bout of cellulitis at the fairgrounds (Summer 2014)

We noticed as we unloaded Diva that her right hind leg was looking a bit swollen. Ten minutes after that, the entire leg had swelled up so badly we had to call out an emergency vet (on a holiday weekend no less).

We discovered that Diva had experienced a bout of cellulitis, which is a bacterial infection that causes extreme swelling in even the smallest of wounds in horses. After weeks of diligent rehab by us and with the guidance of our vet, Diva was able to be shown at the Indiana State Fair, where she, amazingly, placed in the top five in every class of 30+ horses!



Diva returning to showing (Fall 2014)

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But this luck was short-lived. Diva experienced another bout of cellulitis the next summer, right as I was leaving to begin my freshman year of college. While this was difficult and required a trickier bout of treatment due to the antibiotic-resistant bacterial infection, Diva still remained sound in spite of the odds. Even with all of the catheters, needles, antibiotics, etc., Diva never became angry nor lashed out at anyone. It was almost as if she knew that we were all there to help her.



Hock injury-Diva at Purdue Veterinary Hospital (May 2018), preventatively treating infection due to history

Of course, according to Murphy's Law, something that can go wrong, did. Not cellulitis this time, thank goodness! In May 2018, Diva experienced a freak accident in which she cut her hock, on her "bad" right hind leg that had already experienced all of the cellulitis flare-ups. We decided a trip to

Purdue University Large Animal Veterinary Clinic* was the best way to treat her in a sterile environment. After x-rays and tests galore, it was determined that although the cut was very deep, it missed (by a few cm) any major structures in her hock joint and ligaments. After yet more months of rehab, both at Purdue and at home, vets were skeptical that Diva would ever return to her same level of soundness. We were told that her vet team would be happy for her, at 15 years old, to be only 70% sound for the rest of her life.

While we love Diva and were prepared for this result, we are thrilled to report that Diva has been 100% sound for over a year now! Our vet was still shocked when she came out for her annual check-up this spring, saying that she knew of at least two other of her patients who experienced similar injuries and now were permanently lame. We are extremely thankful for Diva's fighting spirit and are hopeful that we will spend many more years taking on new challenges together. It just goes to show that even after injuries, with the right care and a lot of hope, horses can come through on the other side and return to their roles or, in some cases, step into new ones.

*Funded Research at this institution



Showmanship class Indiana State Fair August 2018 with my sister, Rachel, for her 10th year and final show of 4-H

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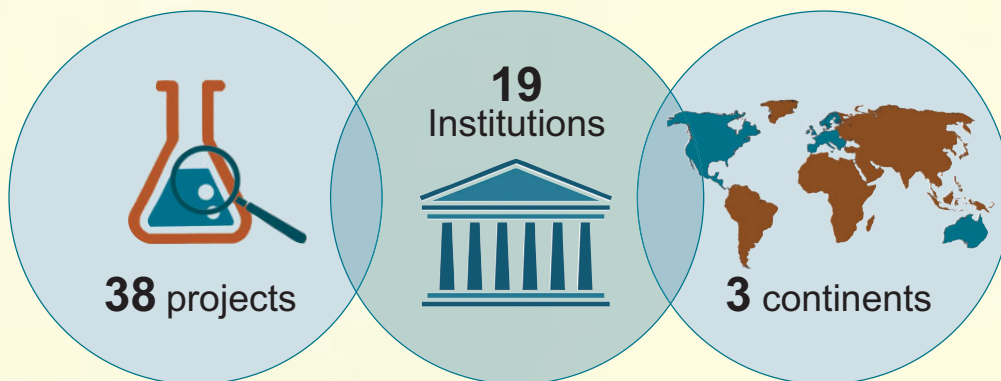
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-Dr. Larry Bramlage
Orthopedic Surgeon
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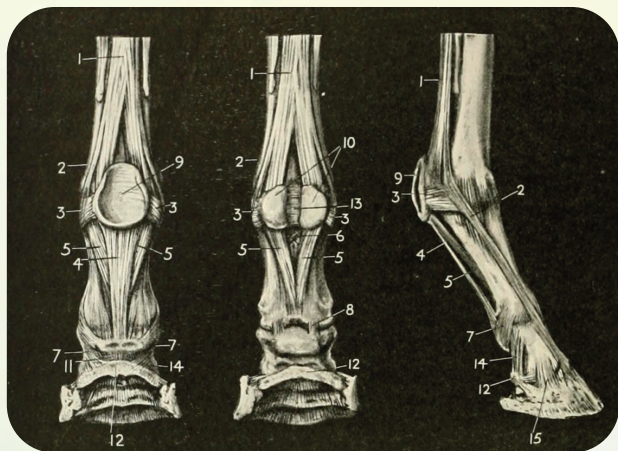
A Clinician's Success Story

This case study was submitted to the foundation by

By **Jennifer C. Jordan, VMD DACVS**

Rood and Riddle Equine Hospital • Lexington, KY/ Wellington, FL

A 13-year-old Warmblood stallion used for show jumping was examined for chronic right forelimb lameness and a history of pain on lower limb flexion. Physical examination was unremarkable. The horse was deemed to be 1.5 degrees lame in the right forelimb when trotted in-hand. A marked painful response was observed following lower limb flexion of the right forelimb. Following an intra-articular (joint) block of the right front fetlock the horse's lameness resolved but the flexion remained more positive than the contralateral limb. The response to flexion improved following addition of a palmar digital nerve block. Radiographs of the right front fetlock were unremarkable. Ultrasound examination of the palmar pastern region revealed suspicious changes in the medial oblique distal sesamoidean ligament (ODSL); however, these were not sufficiently convincing to make a diagnosis.



High field MRI revealed increased signal intensity and enlargement of both the lateral and medial ODSL. An IV regional limb perfusion with dental pulp derived stem cells was performed and a prolonged rest and rehabilitation program was initiated. Specifically, the horse underwent 90 days of stall rest with hand grazing,

followed by another 60 days of stall rest with hand/tack walking. The period of stall rest was somewhat (30 days) longer than is customary because at the horse's 30-day recheck his response to lower limb flexion was still positive.

After five months of rest the stallion gradually resumed trot work under saddle. After two months he was trotting 40 minutes daily. Throughout this rehabilitation process the horse's soundness was monitored carefully and serial monitoring of the ultrasonographic appearance of the affected ligaments was performed. Routine joint maintenance was performed prior to resumption of full flat work, and turnout was re-introduced (seven months from the time of diagnosis). The horse returned to the show ring 11 months from original examination and resumed international-level (FEI) competition two months later. In the 12 months following his return to competition the horse has continued to earn top placings in national and international grand prix competition.

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