



Equine athletes are tasked with traveling at high speeds, which means a healthy respiratory tract is a requisite for success

Taking a Deep Breath

EQUINE ATHLETIC PERFORMANCE TIED TO RESPIRATORY HEALTH

By AMANDA DUCKWORTH

IN THE EQUINE world, many are familiar with the adage “no hoof, no horse,” but when it comes to Thoroughbreds, having a well-functioning respiratory system is also vital for any chance of finding the winner’s circle. Simply put, it is hard to be the fastest when breathing becomes difficult.

Understanding both common respiratory issues as well as how respiratory muscles develop during intense training gives everyone a better understanding of

how to manage racehorses. Because of the importance of the respiratory tract for all horses, but especially equine athletes, it is no surprise that it is a highly studied and evolving area of research.

Unfortunately, respiratory problems are not unusual in horses. Troubles can range from infectious diseases such as viral infections and strangles to non-infectious issues such as asthma and laryngeal hemiplegia. In February 2022, *Animals (Basel)* published “Advances

in the Diagnosis of Equine Respiratory Diseases: A Review of Novel Imaging and Functional Techniques.”

“Respiratory problems are common in horses and are often diagnosed as a cause of poor athletic performance,” researchers explained. “The basic diagnostic techniques of the equine respiratory tract examination are not always sufficient for a complete diagnosis of the disease, its exacerbation, remission, or response to treatment. Therefore, advances have been introduced in the diagnosis of equine respiratory diseases.

“Among them, we can distinguish the high-resolution imaging modalities like computed tomography (CT) and magnetic resonance (MR) imaging. These techniques have revolutionized the capability of visualizing detailed anatomy of the upper respiratory tract, offering the practitioners an advanced view of airway pathology and allowing for appropriate management planning.”

Beyond advancements in diagnostics, how equine athletes are affected by breathing issues continues to be researched. In June 2022 *Animals (Basel)* published “Upper and Lower Airways Evaluation and Its Relationship with Dynamic Upper Airway Obstruction in Racehorses.”

“Horses are obligatory nasal breathers and cannot avoid the high pressures occurring at the level of the nasopharynx during exercise by switching to oral breathing like other species,” explained researchers. “Dynamic upper airway obstructions (DUAO) are common in racehorses, but their pathogenetic mechanisms have not been completely clarified yet. Multiple studies suggest that alterations of the pharyngo-laryngeal region visible at resting endoscopy may be predictive of the onset of DUAO, and the development of DUAO may be associated with pharyngeal lymphoid hyperplasia (PLH), lower airway inflammation (LAI), and exercise-induced pulmonary hemorrhage (EIPH).”

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HEALTH ZONE

Respiratory

For this retrospective study, researchers investigated the possible relationship between the findings of a complete resting evaluation of the upper and lower airways and DUAO. In total, 360 racehorses, a mix of both Standardbreds and Thoroughbreds, who were all referred for poor performance or abnormal respiratory noises, were enrolled in the study. They underwent a diagnostic protocol including resting and high-speed treadmill endoscopy (HSTE), cytological examination of the bronchoalveolar lavage fluid, and radiographic assessment of the epiglottis length.

“DUAOs were more commonly observed in Thoroughbred racehorses than in Standardbred racehorses, confirming a possible breed predisposition,” researchers concluded. “Conversely, age






From research analyzing the breathing capacity of horses during training, researchers concluded: “The demands of the respiratory system increase substantially during exercise, and this system is thought to be the limiting factor which determines athletic performance.”

did not seem to influence the onset of DUAO on HSTE, as pharyngo-laryngeal alterations were detected more frequently in younger horses only at resting upper

airway endoscopy. The detection, at resting endoscopy, of the abnormal appearance and function of the pharyngo-laryngeal region was associated with the

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development of DUAO: in particular, a flaccid appearance of the epiglottis, with a loss of convexity and rigidity, was associated with the occurrence of DDSP (dorsal displacement of the soft palate) both at rest and on HSTE.

“In contrast, the epiglottis length measured radiographically was not associated with DUAO, suggesting that the epiglottis may be involved in maintaining the stability of the upper respiratory tract, not based on its dimensions but on its conformation. Finally, in the present study, no association was observed between DUAO and the inflammation of the upper and lower airways, nor between DUAO and EIPH.”

Researchers have also been exploring how to help horses who have faced issues find ways to successfully train. In September 2021, The Veterinary Journal published “Inspiratory muscle training for the treatment of dynamic upper airway collapse in racehorses: A preliminary investigation.”

“Exercise-induced upper airway collapse (UAC) probably occurs when the stabilizing muscles of the upper airway are unable to withstand the dramatic changes in airflow and pressure that occurs during exercise,” researchers explained. “In racehorses, the mainstay of treatment is surgical intervention. In human athletes, exercise-induced laryngeal obstruction has been treated successfully with inspiratory muscle training (IMT). The aims of this study were to assess the feasibility of IMT in racehorses and describe the exercising endoscopy findings pre- and post-IMT in racehorses diagnosed with dynamic UAC.”

For the study, 17 horses were able to successfully complete the IMT protocol, while full information is available on 10 of them. They wore a mask with an



One study made a connection between gluteal muscle size based on whether a horse had airway surgery or not

THE RESPIRATORY SYSTEM OF THOROUGHBREDS IS AS COMPLEX AS IT IS VITAL TO THEIR SUCCESS ON THE TRACK. RESEARCH CONTINUES TO STUDY THE BEST PRACTICES IN TERMS OF DIAGNOSIS, TRAINING, AND REHABILITATION.

attached threshold-valve to apply an additional load during inspiration, creating a training stimulus with the purpose of increasing upper airway muscle strength. Researchers reported that each horse underwent IMT once daily, while standing in the stable, five to six days per week for 10 weeks. Then, endoscopy recordings were analyzed in a blinded manner using an objective grading scheme and subjective pairwise analysis.

“The results of this investigation demonstrate that the application of IMT in horses diagnosed with UAC was feasible,” researchers concluded. “Objective grading analysis showed a lower grade of vocal fold collapse (6/9 horses), palatal instability (7/10 horses), and

intermittent dorsal displacement of the soft palate (5/7 horses) post-IMT. Pairwise subjective analysis suggested better overall airway function post-IMT in 3/10 horses. The main limitations of this preliminary investigation were the low number of horses examined and lack of a control population. Further research is required to investigate the effects of IMT on upper airway muscle strength and to evaluate its efficacy

for prevention and treatment of UAC.”

As well as expanding knowledge when something goes wrong, technology is also helping advance the understanding of what Thoroughbreds are naturally working with and how their respiratory muscles are impacted by the type of training they undergo. In March 2023, the Equine Veterinary Journal published “Training the equine respiratory muscles: Ultrasonographic measurement of muscle size” as well as “Training the equine respiratory muscles: Inspiratory muscle strength,” which were conducted by the same researchers.

“Limited information exists regarding changes in the size of respiratory and locomotor muscles in response to exercise training in the Thoroughbred racehorse,” explained researchers. “The demands of the respiratory system increase substantially during exercise, and this system is thought to be the limiting factor which determines athletic performance.”

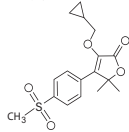
For the first study, researchers aimed to describe and compare the responses of the respiratory and locomotor muscles to conventional exercise training and inspiratory muscle training (IMT) using a prospective randomized controlled trial. To do so, they used Thoroughbred racehorses in training for National Hunt races from two

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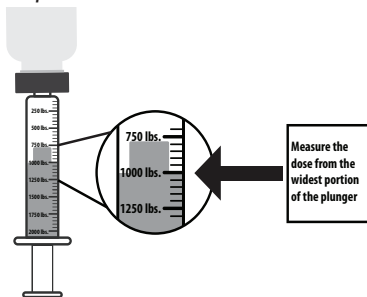
Each 1.25 mL volume will treat 250 pounds of body weight and each additional 0.25 mL volume corresponds to approximately a 50 lb weight increment. The provided dosing syringe is calibrated so that each line corresponds to a 50 lb weight increment. To deliver the correct dose, round the horse's body weight up to the nearest 50 pound increment (if the body weight is an exact 50 pound increment, do not round up).

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EquiCoxib Oral Dosing Guide

Body Weight (lb)	Dose Volume (mL)
250	1.25 mL
500	2.5 mL
750	3.75 mL
1000	5 mL
1250	6.25 mL

- 1) Remove draw-off cap. Peel off the foil-backed seal from the bottle.
- 2) Screw the draw-off cap tightly back on the bottle.
- 3) Remove the seal from the top of the cap exposing the cross-hatched opening in the center of the silicone liner.
- 4) Remove the provided oral dosing syringe from its plastic cover.
- 5) Insert the oral dosing syringe firmly into the cross-hatched opening of the cap's silicone liner.
- 6) Turn the bottle with attached syringe upside down. Pull back the syringe plunger until the widest portion of the plunger lines up with the line that corresponds with the animal's weight. Each line between the 250 lb increments corresponds to 50 lb.



- 7) Turn the bottle with attached syringe right side up and separate the dosing syringe from the bottle.
- 8) Give orally according to your veterinarian's instructions. **DO NOT INJECT.**

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Animal Safety: Clients should be advised to observe for signs of potential drug toxicity and be given a Client Information Sheet with each prescription. Keep EquiCoxib in a secure location out of reach of dogs, cats, and other animals to prevent accidental ingestion or overdose.

To report suspected adverse drug events, for technical assistance or to obtain a copy of the Safety Data Sheet (SDS), contact Aurora Pharmaceutical at 1-888-215-1256 or www.aurorapharmaceutical.com. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at www.fda.gov/reportanimalae.

Precautions:

Horses should undergo a thorough history and physical examination before initiation of NSAID therapy. Appropriate laboratory tests should be conducted to establish hematological and serum biochemical baseline data before and periodically during administration of any NSAID. Clients should be advised to observe for signs of potential drug toxicity and be given a Client Information Sheet with each prescription. See **Information for Owner or Person Treating Horse** section of this package insert.

Treatment with EquiCoxib should be terminated if signs such as inappetence, colic, abnormal feces, or lethargy are observed. As a class, cyclooxygenase inhibitory NSAIDs may be associated with gastrointestinal, renal, and hepatic toxicity. Sensitivity to drug-associated adverse events varies with the individual patient. Horses that have experienced adverse reactions from one NSAID may experience adverse reactions from another NSAID. Patients at greatest risk for adverse events are those that are dehydrated, on diuretic therapy, or those with existing renal, cardiovascular, and/or hepatic dysfunction. Concurrent administration of potentially nephrotoxic drugs should be carefully approached or avoided. NSAIDs may inhibit the prostaglandins that maintain normal homeostatic function. Such anti-prostaglandin effects may result in clinically significant disease in patients with underlying or pre-existing disease that has not been previously diagnosed. Since many NSAIDs possess the potential to produce gastrointestinal ulcerations and/or gastrointestinal perforation, concomitant use of EquiCoxib Oral Solution with other anti-inflammatory drugs, such as NSAIDs or corticosteroids, should be avoided. The concomitant use of protein bound drugs with EquiCoxib Oral Solution has not been studied in horses. The influence of concomitant drugs that may inhibit the metabolism of EquiCoxib Oral Solution has not been evaluated. Drug compatibility should be monitored in patients requiring adjunctive therapy. The safe use of EquiCoxib Oral Solution in horses less than one year in age, horses used for breeding, or in pregnant or lactating mares has not been evaluated. Consider appropriate washout times when switching from one NSAID to another NSAID or corticosteroid.

Adverse Reactions: In controlled field studies, 127 horses (ages 3 to 37 years) were evaluated for safety when given firocoxib at a dose of 0.045 mg/lb (0.1 mg/kg) orally once daily for up to 14 days. The following adverse reactions were observed. Horses may have experienced more than one of the observed adverse reactions during the study.

Adverse Reactions Seen in U.S. Field Studies Firocoxib was safely used concomitantly with other therapies, including vaccines, anthelmintics, and antibiotics, during the field studies. The safety data sheet (SDS) contains more detailed occupational safety information.

To report suspected adverse drug events, for technical assistance, or to obtain a copy of the Safety Data Sheet (SDS), contact Aurora Pharmaceutical Inc. at 1-888-215-1256 or www.aurorapharmaceutical.com. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS, or online at www.fda.gov/reportanimalae.

Adverse Reactions	Firocoxib n=127	Active Control n=125
Abdominal pain	0	1
Diarrhea	2	0
Excitation	1	0
Lethargy	0	1
Loose stool	1	0
Polydipsia	0	1
Urticaria	0	1

Information for Owner or Person Treating Horse: You should give a Client Information Sheet to the person treating the horse and advise them of the potential for adverse reactions and the clinical signs associated with NSAID intolerance. Adverse reactions may include erosions and ulcers of the gums, tongue, lips and face, weight loss, colic, diarrhea, or icterus. Serious adverse reactions associated with this drug class can occur without warning and, in some situations, result in death. Clients should be advised to discontinue NSAID therapy and contact their veterinarian immediately if any of these signs of intolerance are observed. The majority of patients with drug-related adverse reactions recover when the signs are recognized, drug administration is stopped, and veterinary care is initiated.

Clinical Pharmacokinetics / Pharmacodynamics: Pharmacokinetics: When administered as a 0.045 mg/lb (0.1 mg/kg) dose in oral paste to adult horses with normal access to roughage, feed, and water, the absolute bioavailability of firocoxib from oral paste is approximately 79%. Following oral administration, drug peak concentration (C_{max}) of 0.08 mcg/mL can be reached at 4 hours (T_{max}) post-dosing. However, in some animals, up to 12 hours may be needed before significant plasma concentrations are observed. Little drug amount distributes into blood cells. The major metabolism mechanism of firocoxib in the horse is decyclopropyl-methylation followed by glucuronidation of that metabolite. Based upon radiolabel studies, the majority of firocoxib is eliminated in the urine as the decyclopropylmethylated metabolite. Despite a high rate of plasma protein binding (98%), firocoxib exhibits a large volume of distribution (mean Vd(ss) = 1652 mL/kg). The terminal elimination half-life (T_{1/2}) in plasma averages 30-40 hours after IV or oral paste dosing. Therefore, drug accumulation occurs with repeated dose administrations and steady state concentrations are achieved beyond 6-8 daily oral doses in the horse. Dose linearity exists from 1X-2X of 0.1 mg/kg/day.

Mode of action: EquiCoxib (firocoxib) is a cyclooxygenase-inhibiting (coxib) class, non-narcotic, non-steroidal anti-inflammatory drug (NSAID) with anti-inflammatory, analgesic and antipyretic activity¹ in animal models. Based on in vitro horse data, firocoxib is a selective inhibitor of prostaglandin biosynthesis through inhibition of inducible cyclooxygenase-2 isoenzyme (COX-2)². Firocoxib selectivity for the constitutive isoenzyme, cyclooxygenase-1 (COX-1) is relatively low. However, the clinical significance of these in vitro selectivity findings has not been established.

Effectiveness: Two hundred fifty-three client-owned horses of various breeds, ranging in age from 2 to 37 years and weighing from 595 to 1638 lbs, were randomly administered firocoxib oral paste or an active control drug in multi-center field studies. Two hundred forty horses were evaluated for effectiveness and 252 horses were evaluated for safety. Horses were assessed for lameness, pain on manipulation, range of motion, joint swelling, and overall clinical improvement in a non-inferiority evaluation of firocoxib oral paste compared to an active control. At study's end, 84.4% of horses treated with firocoxib oral paste were judged improved on veterinarians' clinical assessment, and 73.8% were also rated improved by owners. Horses treated with firocoxib oral paste showed improvement in veterinarian-assessed lameness, pain on manipulation, range of motion, and joint swelling that was comparable to the active control.

Animal Safety: In a target animal safety study, firocoxib was administered orally to healthy adult horses (two male castrates and four females per group) at 0, 0.1, 0.3 and 0.5 mg firocoxib/kg body weight (1, 3 and 5X the recommended dose) for 30 days. Administration of firocoxib at 0.3 and 0.5 mg/kg body weight was associated with an increased incidence of oral ulcers as compared to the control group but, no oral ulcers were noted with 0.1 mg/kg. There were no other drug-related adverse findings in this study.

In another target animal safety study, firocoxib was administered orally to healthy adult horses (four males or male castrates and four females per group) at 0, 0.1, 0.3 and 0.5 mg firocoxib/kg body weight (1, 3 and 5X the recommended dose) for 42 days. Administration of firocoxib at 0.1, 0.3 and 0.5 mg/kg body weight was associated with delayed healing of pre-existing oral (lip, tongue, gingival) ulcers. In addition, the incidence of oral ulcers was higher in all treated groups as compared to the control group.

Clinical chemistry and coagulation abnormalities were seen in several horses in the 0.5 mg/kg (5X) group. One 5X male horse developed a mildly elevated BUN and creatinine over the course of the study, prolonged buccal mucosal bleeding time (BMBT), and a dilated pelvis of the right kidney. Another 5X male had a similar mild increase in creatinine during the study but did not have any gross abnormal findings. One female in the 5X group had a prolonged BMBT, bilateral tubulointerstitial nephropathy and bilateral papillary necrosis. Tubulointerstitial nephropathy occurred in one 3X female, two 3X male horses, and the 5X female horse discussed above with the prolonged BMBT. Papillary necrosis was present in one 1X male horse and the 5X female horse discussed above. Despite the gross and microscopic renal lesions, all of the horses were clinically healthy and had normal hematology, clinical chemistry and urinalysis values.

In another target animal safety study, firocoxib was administered orally to healthy adult horses (three females, two male castrates and one male per group) at 0, 0.25 mg/kg, 0.75 mg/kg and 1.25 mg/kg (2.5, 7.5 and 12.5X the recommended dose of 0.1 mg/kg) for 92 days. An additional group of three females, two male castrates and one male per group, was dosed at 1.25 mg/kg for 92 days but was monitored until Days 147-149. There were treatment-related adverse events in all treated groups. These consisted of ulcers of the lips, gingiva and tongue and erosions of the skin of the mandible and head. Gross and microscopic lesions of the kidneys consistent with tubulointerstitial nephropathy were seen in all treated groups. Papillary necrosis was seen in the 2.5X and 12.5X groups. In addition, several 12.5X horses had elevated liver enzymes (GGT, SDH, AST and ALT). One 2.5X horse had increased urine GGT and urine protein levels which was due to renal hemorrhage and nephropathy. Gastric ulcers of the margo plicatus and glandular area were more prevalent in the 2.5X and 7.5X groups, but not seen in the 12.5X group. The group of horses that were monitored until Days 147-149 showed partial to full recovery from oral and skin ulcers, but no recovery from tubulointerstitial nephropathy.

Storage Information: Store below 77°F (25°C). Brief excursions up to 104°F (40°C) are permitted.

How Supplied: EquiCoxib is available in bottles containing 90 mL of EquiCoxib Oral Solution, sufficient to treat a 1250 lb horse for up to 14 days.

References: ¹McCann ME, Rickes EL, Hora DF, Cunningham PK et al. In vitro effects and in vivo efficacy of a novel cyclooxygenase-2 inhibitor in cats with lipopolysaccharide-induced pyrexia. *Am J Vet Res.* 2005 Jul;66 (7):1278-84

²McCann ME, Anderson DR, Brideau C et al. In vitro activity and in vivo efficacy of a novel COX-2 inhibitor in the horse. *Proceedings of the Academy of Veterinary Internal Medicine.* 2002. Abstract 114, p.789.

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different training yards. The horses were required to be “unfit” but healthy and to not have undergone any routine exercise for a minimum of eight weeks before the first examination. In all, 79 horses were recruited, with 43 coming from the first yard, and 36 from the second.

Ultrasonographic images were obtained for selected muscles of the upper airway, diaphragm, accessory respiratory, and locomotor systems and their sizes measured. For the qualifying horses, exams were done three separate times: when unfit (A), following 12 weeks of conventional exercise training (B), and following 10-12 weeks continued training at race fitness (C). Furthermore, horses at the first yard performed IMT between the second and third timepoints and were randomly assigned into high-load (treatment) or low-load (control) group.

“Upper airway muscle size increased in response to conventional race training between timepoints A-C and B-C,” researchers concluded. “Diaphragm size increased in response to conventional exercise training between timepoints A and B. The diaphragm size of horses that undertook high-load IMT was either maintained or increased, whereas diaphragm size decreased in horses that undertook low-load IMT or no IMT between timepoints B and C. A significant interaction between gluteal muscle size and airway surgery status was observed, with greater gluteal muscle thicknesses measured in horses that had not previously undergone airway surgery.

“Overall, ultrasonographic examination is an easy and non-invasive method to obtain information about skeletal muscle changes in response to a training stimulus. Conventional exercising training increases the thickness of both



Horses breathe through their nostrils and can't mitigate the high pressures occurring in the nasopharynx during exercise by turning to oral breathing like other species

locomotor and respiratory muscles in the Thoroughbred racehorse. In addition, IMT increases the thickness of the diaphragm. The association between diaphragm thickness and race performance warrants further investigation in a larger number of horses, along with locomotor muscle and cardiac measurements.”

For the second study, researchers wanted to measure an index of inspiratory muscle strength (IMSi) before and after a period of conventional exercise training (phase 1) and inspiratory muscle training (IMT), comparing high-load (treatment) and low-load (control)

groups (phase 2).

During phase 1, 20 Thoroughbreds were asked to complete an inspiratory muscle strength test (IMST) twice on two occasions. This occurred first in July when they were unfit and again in October when race fit. During phase 2, 35 Thoroughbreds were randomly assigned to either a high-load or low-load group. The IMST was performed twice on two occasions, timepoint B (October) and timepoint C (January). Conventional exercise training and racing continued during the study period.

“This investigation is the first to demonstrate a significant increase in inspiratory muscle strength in Thoroughbred racehorses following 12 weeks of conventional exercise training for National Hunt racing,” researchers concluded. “These results are in line with similar investigations conducted in human athletes. Following a 10-week period of IMT there was a further significant increase in inspiratory muscle strength in the high-load (treatment) group, but not in the low-load (control) group. Alongside this, there were significant increases in the power, work, and volume in the high-load group.

“In conclusion, the results of this investigation show that the prevalence of behavioral abnormalities during IMT and IMST is low, and that there is an increase in inspiratory muscle strength in response to both conventional race training and high-load IMT. Further investigation into the association between inspiratory muscle size, such as the diaphragm, and other physiological performance variables are required to help determine the optimal method for training racehorses to achieve peak performance while maximizing health and welfare.”



Dynamic upper airway obstructions, detected through endoscopes, are common in racehorses, but research suggests that the “pathogenetic mechanisms have not been completely clarified yet.”

The above studies used a mix of mares and geldings for the research. Another recent study investigated the inherent differences between the sexes when it comes to the respiratory tract. In November 2023, Veterinary Journal published “Comparison of ventilatory and oxygen consumption measurements of yearling Thoroughbred colts and fillies exercising unriden on an all-weather track.”

“Sex effects on ventilatory and oxygen consumption ($\dot{V}O_2$) measurements during exercise have been identified in humans,” explained researchers. “This study’s aim was to evaluate the hypothesis that there are sex effects on ventilatory and $\dot{V}O_2$ measurements in exercising untrained yearling Thoroughbreds.”

A total of 41 Thoroughbreds were used

in the study, 16 colts and 25 fillies. They were all under the same management. Yearlings that were included had been broken to be ridden and introduced to the gallops but had not begun ridden exercise training. All of them were sound and healthy before exercise testing began. For the study, physiological, ventilatory, and exercise data were gathered from horses exercising unriden at high intensity on an all-weather track from a global positioning-heart rate unit and a portable ergospirometry system.

“Ventilation in yearling Thoroughbreds differed between sex groups, with colts obtaining greater airflow rates and absolute but not mass specific volumes,” researchers concluded. “However, fillies had a greater mass specific $\dot{V}O_2$ peak than colts, likely due to differences in

body weight. Given their morphological differences, it is likely that lung volumes and airway diameters are smaller for fillies, resulting in greater resistance and lower air flows and absolute volumes during exercise.

“Further research is required to investigate the ventilatory and potential pulmonary morphological differences between Thoroughbred sex groups and how these differences may change with maturation and impact performance, especially in the presence of upper and/or lower airway obstructive disorders.”

The respiratory system of Thoroughbreds is as complex as it is vital to their success on the track. Research continues to study the best practices in terms of diagnosis, training, and rehabilitation. **BH**

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