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**Rural Industries Research and  
Development Corporation**

# **Exercise-Induced Pulmonary Haemorrhage in Thoroughbred Racehorses**

**Effects on racing performance**

**A report for the Rural Industries Research  
and Development Corporation**

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# Foreword

Exercise-induced pulmonary haemorrhage occurs in most thoroughbred race horses. The overall objective of this study was to determine whether exercise-induced pulmonary haemorrhage (EIPH) is detrimental to athletic performance of thoroughbred racehorses. Treatment and prevention of EIPH incurs considerable cost to the Australian racing industry. However, the importance of EIPH in reducing race performance or in limiting career achievement or earnings of racehorses has not been documented. In short, the importance of this disorder has not been demonstrated. Demonstration of the impact of EIPH on performance of Australian thoroughbred racehorses would allow:

- Appropriate allocation of resources to further investigation of EIPH, including investigation of prevention and treatment of the disorder.
- Permit owners, trainers and veterinarians to make informed decisions regarding the training, racing and veterinary management of horses with EIPH.
- Permit racing authorities to make informed decisions regarding rules dealing with horses with EIPH and epistaxis.

To this end, we used short term (performance in a race) indicators of athletic performance to determine if EIPH adversely affects athletic potential of thoroughbred racehorses. Presence of EIPH and its severity was determined by endoscopic tracheobronchial examination of thoroughbred racehorses between 30 and 120 minutes after racing at Metropolitan race tracks in Victoria. Seven hundred and forty four thoroughbred racehorses of both sexes were examined. Tracheobronchial examination was recorded on videotape and the severity of haemorrhage subsequently determined by 3 observers blinded to the horse's identity and race performance. Details of race performance, demographics, and other variables potentially influencing performance and measures of career quality (starts, career earnings, career duration) were abstracted from the race records. The relationship between EIPH and performance was determined using principal component analysis as previously described by us.

This project was funded from industry revenue which is matched by funds provided by the Federal Government.

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## **Tony Bryne**

Acting Managing Director

Rural Industries Research and Development Corporation

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# Executive Summary

Exercise-induced pulmonary haemorrhage (EIPH) is a condition with high prevalence in racing thoroughbreds. However, despite its perceived importance as a cause of morbidity and impaired performance, few studies have attempted to address the relationship of EIPH to race performance. Although many horsemen and veterinarians consider EIPH to be an important cause of poor performance, studies that have examined this relationship have not detected statistically significant relationships between EIPH and racing performance. Thus, the current study was conducted to investigate the association between performance and EIPH in a large number of thoroughbred race horses.

Endoscopic examinations were performed on 744 horses, representing 52.1% of those eligible horses starting during the study period. Both presence of EIPH and its severity were significantly ( $P < 0.05$ ) associated with race performance. Horses with EIPH, defined as grade 2 or higher, were 4.0 times less likely to win, 1.8 times less likely to finish in the top 3 places, and finished 1.8 meters farther behind the winner than did unaffected horses. The severity of EIPH (grade 0-4) was significantly associated with reduced probability of winning, slower race time normalized to race length of 1200 meters, lower horse speed, and greater length behind the winner. Horses with grade 4 EIPH finished an average of 3.4 meters farther behind the winner than horses of grade 0.

These results demonstrate that EIPH has a significant negative relationship with race performance of thoroughbred horses. There is a proportional inverse relationship between severity of EIPH and performance. There was no evidence that EIPH was associated with superior performance. The results of this study therefore provide practitioners with valuable information regarding the effect of EIPH on performance of thoroughbred race horses that are not administered furosemide. Exercise-induced pulmonary haemorrhage is a cause of reduced performance in thoroughbred race horses.

# 1. Tracheobronchoscopic assessment of exercise-induced pulmonary haemorrhage in thoroughbred race horses.

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Acknowledgements: Supported by Racing Victoria Ltd., Rural Industries Research and Development Corporation (Australia), University of Melbourne and The Ohio State University. The cooperation of thoroughbred owners and trainers in Victoria, Australia is gratefully acknowledged. The expert technical assistance of Elli Jellet is gratefully acknowledged.

## Summary:

Exercise-induced pulmonary haemorrhage is a pervasive condition in thoroughbred race horses. Detailed investigation of causes, effects and treatment of EIPH requires methods to assess the severity of haemorrhage. An important attribute of a grading system is that there be minimal inter-observer variability. We tested the inter-observer concordance for grading severity of EIPH in thoroughbred race horses by tracheobronchoscopic examination. Agreement among the 3 observers using a 5 level scoring system of EIPH detected during tracheobronchoscopic examination of 747 thoroughbred race horses within 2 hours of racing was excellent. All 3 observers agreed or 2 of 3 agreed and the third differed by one grade in 99.4% of observations. This study demonstrates the high degree of inter-observer reliability in tracheobronchoscopic assessment of severity of EIPH in thoroughbred horses.

## Introduction:

Exercise-induced pulmonary haemorrhage (EIPH) is a pervasive condition of thoroughbred race horses.<sup>1,2</sup> Determination of the importance of EIPH, in terms of athletic performance, well being of horses, investigation of the role of putative risk factors, and examination of the efficacy of treatment requires a method of assessment of severity of haemorrhage that is highly repeatable between observers. Techniques used to assess the severity of EIPH include measurement of red blood cell count in bronchoalveolar lavage fluid or subjective assessment of the severity of haemorrhage based on the presence of blood in airways detected during tracheobronchoscopic examination.<sup>1,3-5</sup> Tracheobronchoscopic assessment of severity of EIPH offers the advantage of immediacy, in that handling and laboratory processing of samples is not necessary, and simplicity. However, previous descriptions of the use of tracheobronchoscopic assessment of severity of EIPH have not reported on the inter-observer reliability of the technique. The purpose of the current study was to determine the inter-observer reliability of tracheobronchoscopic assessment of severity of exercise-induced pulmonary hemorrhage in thoroughbred race horses.

## Materials and methods:

Study design: The inter-rater reliability of tracheobronchoscopic assessment of severity of exercise-induced pulmonary haemorrhage in thoroughbred horses was investigated in an observational study of a convenience sample of horses. Eight hundred and fifty endoscopic examinations were performed on 747 thoroughbred race horses.

Horses: Tracheobronchoscopic examinations were performed on thoroughbred horses within 2 hours of competing in a race. Races were 1000 – 3200 meter flat races run on turf at Flemington, Moonee Valley, Caulfield and Sandown race tracks in Melbourne, Australia between March 1 and June 18, 2003.

Examinations: Tracheobronchoscopic<sup>a</sup> examinations of the upper airways, pharynx, larynx, trachea and carina were performed on unsedated horses restrained by use of a nose twitch and halter. The nasopharynx and trachea to the level of the tracheal bifurcation were examined for the presence of blood. The examination was recorded on videotape for subsequent review. The videotaped examinations were independently reviewed by 3 veterinarians (JB, AD, KH) and the severity of exercise-induced pulmonary haemorrhage graded according to modifications of described grading systems.<sup>1,3</sup> Previously described systems had 4 or 5 grading levels whereas the current modification has 5 (Figure 1):

Grade 0: No blood detected in the pharynx, larynx, trachea or main stem bronchi.

Grade 1: Presence of one or more flecks of blood or  $\leq 2$  short ( $< \frac{1}{4}$  length of the trachea) narrow ( $< 10\%$  of the tracheal surface area) streams of blood in the trachea or main stem bronchi visible from the tracheal bifurcation.

Grade 2: One long stream of blood ( $>$  half the length of the trachea) or  $> 2$  short streams occupying less than  $\frac{1}{3}$  of the tracheal circumference.

Grade 3: Multiple, distinct streams of blood covering more than  $\frac{1}{3}$  of the tracheal circumference. No blood pooling at the thoracic inlet.

Grade 4. Multiple, coalescing streams of blood covering  $> 90\%$  of the tracheal surface. Blood pooling at the thoracic inlet.

Statistical analysis: Weighted kappa statistics were calculated for each combination of observers. Weighted kappa statistics take into account the magnitude of the difference between observers for a particular observation.<sup>6</sup> Disagreement between observers of one grade is considered of less importance than is disagreement by two or more grades. Kappa statistics were considered to indicate poor ( $\kappa < 0.2$ ), fair (.2 to 0.40), moderate (0.41 to 0.60), good (0.61 to 0.80) and excellent ( $> 0.80$ ) agreement.<sup>7</sup> Results are reported as mean and 95% confidence interval.

## **Results:**

Prevalence of EIPH, defined as blood in the trachea or bronchi detected by at least one observer was 68.4%. Weighted kappa statistics for concordance between pairs of observers were 0.76 (0.73 to 0.79, 95% CI), 0.80 (0.77 to 0.83), and 0.75 (0.72 to 0.79). Severity scores were identical for all 3 observers for 68.7% of examinations. The 3 observers uniformly assigned 269 examinations grade 0, 227 grade 1, 63 grade 2, 17 grade 3 and 8 grade 4. Scores of 2 of the 3 observers agreed, and that of the third observer differed by 1 grade, in 30.7% of examinations. Scores of 2 of 3 observers agreed and that of the third observer differed by  $\geq 2$  grades in 0.4% of observations. All 3 observers disagreed in 0.2 % of examinations. Therefore, all observers agreed or 2 of 3 agreed with the third differing by  $\leq 1$  grade in 99.4% of observations.

## **Discussion:**

The results of the current study demonstrate that it is possible to achieve a high degree of concordance among experienced investigators for assessment of severity of exercise-induced pulmonary haemorrhage in thoroughbred race horses. Previous investigators using similar techniques have not provided measures of the inter-observer variability of their assessment of EIPH. Quantification of inter-observer variability is important if grading systems such as the current one are to be used by more than one observer in either clinical or experimental situations. This study has



important implications for study of EIPH in that it validates the use of a subjective scoring system, thereby providing a tool with which to investigate the causes and effects of EIPH. A weakness of the current study is that while it provides an ordinal assessment of the severity of EIPH it does not provide a quantitative measure of the amount of haemorrhage.

The concordance between observers in the current study was good as indicated by kappa statistics  $> 0.75$ . However, use of the kappa statistic to assess concordance among observers is problematic when the prevalence of the condition is high.<sup>7,8</sup> This occurs because the kappa statistic is a measure of the agreement between observers that occurs above that expected by chance. For conditions with a high prevalence, the probability that observers will agree simply by chance is greater than if the condition were less prevalent. Because the prevalence of EIPH, especially low grade, was high in the present study, there was a high degree of concordance expected by chance alone and therefore the kappa statistics are a conservative estimate of the agreement between observers.

A more utilitarian evaluation of the agreement between observers is provided by the proportion of observations in which two or more observers agreed, and the extent to which observers disagreed. From a practical view point, differences in EIPH grade of 1 are likely of less importance than are differences of 2 or more. Observers in the current study differed by one grade or less in over 99% of examinations, indicating the excellent concordance among observers using the current grading system.

The current grading system was modelled on described systems.<sup>1,3</sup> The earlier system assigned horses to one of four or five grades including 0, whereas the current system assigned horses to one of five grades. We developed the current grading system when it became apparent after examination of several hundred horses that four grades of severity of haemorrhage, in addition to lack of it, could readily be discerned. While the performance of the previously described grading system has not been reported, the high concordance among observers in the current study validates the use of the current grading system in situations in which there is more than one observer.

It is necessary to have a reliable system to evaluate the potential association of EIPH with performance, the role of putative risk factors in the development of EIPH, and the efficacy of therapeutic or prophylactic interventions, such as administration of furosemide or application of nasal dilator strips. Recently, quantification of haemorrhage has been attempted through measurement of red cell count in fluid obtained by bronchoalveolar lavage.<sup>4</sup> While this technique yields numerical results, in the form of red cells per ml of lavage fluid, and red cell counts vary widely among horses, the relationship between red cell count and severity of haemorrhage has not been determined.

Concerns exist that because this technique samples only a small portion of one lung and haemorrhage may be localized or occur from predominantly one lung,<sup>9</sup> the red cell count in lavage fluid may not provide an accurate indication of overall severity of hemorrhage.<sup>10</sup> Conversely, because the technique samples from the distal airways, as opposed to observation of more rostral airways during endoscopic examination, the lavage technique may detect, and quantify, haemorrhage that is not apparent on endoscopic examination. Finally, collection of bronchoalveolar lavage fluid is invasive, requires sedation of the horse and, often, administration of local aesthetic solutions into the airways. These requirements render the technique impractical for screening large numbers of horses in a short period of time, such as may occur during field studies, and for use in horses in competition for which there are restrictions on use of medications.

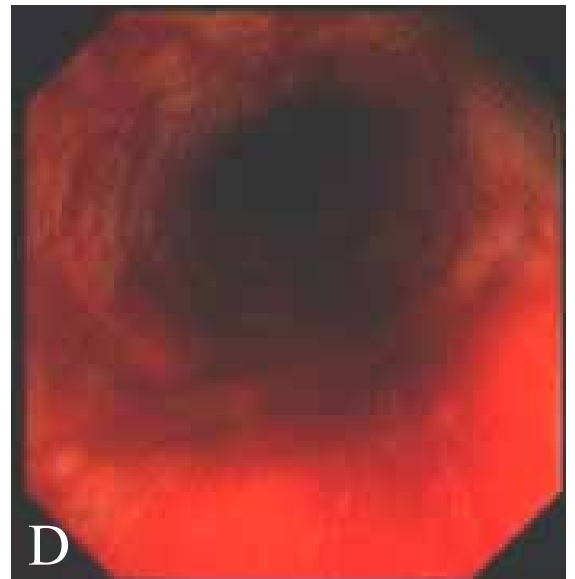
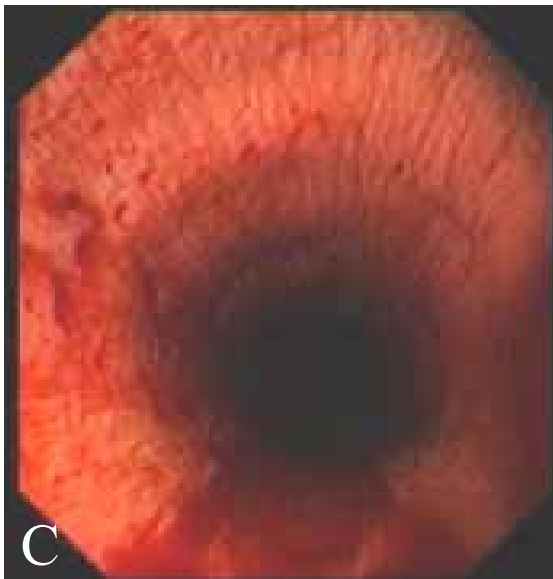
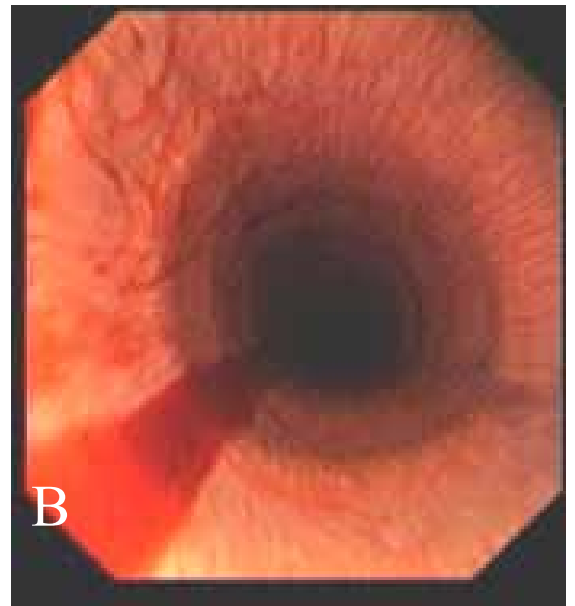
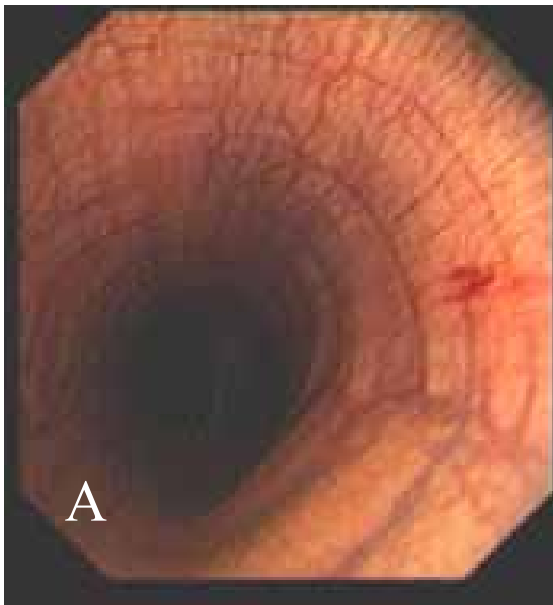
The excellent inter-observer reliability of the grading system described in this study provides a tool for grading severity of EIPH in thoroughbred race horses. Because the grading system is based on tracheobronchoscopic examination of the airways, an examination that can be rapidly and easily performed on unsedated horses after racing, it has the potential to be a valuable tool in the investigation of exercise-induced pulmonary haemorrhage.

**Footnotes**

- a. Olympus Model CF-100TL endoscope, Shirakawa Olympus Co., Ltd., Japan

**Figure legend**

Figure 1. Illustrative examples of grade 1 (A), 2 (B), 3 (C), and 4 (D) pulmonary haemorrhage in thoroughbred race horses. Grade 0, in which blood is not detected during tracheobronchoscopic examination, is not illustrated.



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## 2. Association between exercise-induced pulmonary haemorrhage and performance by thoroughbred race horses

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### **Abstract:**

#### **Objective:**

To investigate the association of EIPH with indices of racing performance in thoroughbred horses not premedicated with furosemide.

#### **Animals:**

744 two to ten year old thoroughbred horses racing in Victoria, Australia.

#### **Study design:**

Prospective, observational cross-sectional study.

#### **Procedure:**

Tracheobronchoscopic examinations were performed on participating horses within 2 hours of racing. Examinations were recorded on videotape and presence and severity (grade 0-4) of EIPH subsequently determined by each of 3 observers masked to the horse's identity. Race records were abstracted for each horse examined. Statistical analysis included discriminant function analysis and logistic regression.

#### **Results:**

0.2% of horses racing and eligible for inclusion in the study were examined. Demographics and performance of the study sample was not significantly different to that of the overall population of horses available for study. Horses with EIPH  $\leq 1$  were 4.03 (1.45 to 14.3, 95% confidence interval,  $P = 0.006$ ) times more likely to win and 1.78 (1.05 to 3.07,  $P = 0.03$ ) more likely to finish in top three places. Horses with EIPH  $\leq 1$  were 3.03 (1.33 to 7.96,  $P = 0.002$ ) times more likely to be in the top 10% of money earned per race, and horses with EIPH finished  $4.36 \pm 1.16$  vs  $2.60 \pm 1.07$  m, ( $P = 0.002$ ) further behind the winner than did unaffected horses.

## **Conclusions and clinical relevance:**

Exercise-induced pulmonary haemorrhage is associated with impaired performance by thoroughbred race horses not premedicated with furosemide. Exercise-induced pulmonary haemorrhage is likely an important cause of poor performance in thoroughbred race horses.

Exercise-induced pulmonary haemorrhage occurs commonly in thoroughbred and Standardbred race horses worldwide. While estimates of the incidence of EIPH after racing vary depending on the population of horses examined, the criteria for diagnosis (epistaxis vs tracheobronchoscopy vs examination of airway washings), and frequency of examination, blood is detected in airways by single tracheobronchoscopic examination in over 50% of thoroughbred horses after racing.<sup>1-3</sup> The high incidence of EIPH has prompted concern and speculation that it is an important cause of impaired performance in thoroughbred race horses. There is a demonstrated association of epistaxis with impaired performance in thoroughbred race horses.<sup>4</sup> However, epistaxis has a low incidence and is usually associated with severe EIPH and the results of these studies may not be relevant to horses with EIPH but not epistaxis. Studies that have employed tracheobronchoscopic examination of thoroughbred horses to detect EIPH have, with one exception, not found an association with performance.<sup>1,2,5-8</sup> However, the ability of these studies to detect an association between EIPH and performance may have been impaired by inadequate statistical power, non-random selection of subjects, and administration of furosemide.

The objective of the current study was to determine if there was an association between presence of EIPH and impaired performance by thoroughbred horses not premedicated with furosemide. Pre-enrolment of horses to minimize chances of selection bias, examination of a large number of horses, and use of statistical techniques to account for confounding and co linearity among variables optimised the statistical power and validity of the study. A secondary objective was to investigate whether there was a relationship between the severity of EIPH and magnitude of effect on indices of performance.

## **Materials and Methods**

### **Design:**

The experiment was a cross-sectional study of thoroughbred race horses. Horses were enrolled in the study before the race in which they were examined. The study design was approved by the animal ethics committee of the University of Melbourne.

### **Experimental methods:**

*Horses:* Horses examined were thoroughbred race horses of either sex competing in flat races at one of four race courses in Melbourne, Victoria, Australia between March 1 and June 18<sup>th</sup>, 2003. Horses raced on turf between 11:30 am and 11:30 pm. Administration of race day medications, including furosemide, is not permitted in thoroughbred racing in Australia and this rule is stringently enforced by application of state-of-the-art drug testing procedures for detection of medicinal and illicit drugs in blood and urine samples. It is therefore unlikely that horses in this study were administered agents that could have affected the development or severity of EIPH.

Horses for study were identified before racing. Prior to the start of the study trainers and owners of thoroughbred race horses were informed of the study by broadcast facsimile of a description of the study to all registered trainers in the state, articles in the trade newsletters and newspapers, articles and interviews in broadcast media, presentations by the investigators at the race tracks and personal contact with opinion making trainers. Identification of horses to be studied on a particular race day was achieved during the 24-48 hours preceding the race. Lists of horses accepted to race were obtained and trainers of eligible horses contacted by telephone to request permission to examine the horse. The risks and benefits of the study were explained and verbal permission

to examine the horse obtained. On the day of racing written informed consent was obtained before the horse raced, the trainer reminded of the study and the horse identified visually by one of the investigators. After racing, horses were brought by handlers to a central location at the race track and the horse examined within 2 hours of racing. One of the investigators ensured that horses listed to be examined were in fact presented for examination.

#### *Detection and quantification of EIPH:*

Exercise-induced pulmonary haemorrhage was detected and quantified by tracheobronchoscopic examination<sup>a</sup> of unsedated horses with 120 minutes of racing. One naris, the nasopharynx, larynx, trachea and carina were examined. The examination was recorded on videotape for subsequent analysis by 3 individuals blinded to the identity of the horse and its race performance.

Severity of EIPH was assessed using a modification of a described system (Hinchcliff et al 2004):

Grade 0: No blood detected in the pharynx, larynx, trachea or main stem bronchi visible from the tracheal bifurcation.

Grade 1: Presence of one or more flecks of blood or  $\leq 2$  short ( $< \frac{1}{4}$  length of the trachea) narrow ( $< 10\%$  of the tracheal surface area) streams of blood in the trachea or main stem bronchi visible from the tracheal bifurcation.

Grade 2: One long stream of blood ( $>$  half the length of the trachea) or  $> 2$  short streams occupying less than  $\frac{1}{3}$  of the tracheal circumference.

Grade 3: Multiple, distinct streams of blood covering more than  $\frac{1}{3}$  of the tracheal circumference. No blood pooling at the thoracic inlet.

Grade 4. Multiple, coalescing streams of blood covering  $> 90\%$  of the tracheal surface with pooling of blood at the thoracic inlet.

#### *Racing records:*

Race records were retrieved from a IRIS, a commercial database maintained by Victoria Racing Ltd. Variables abstracted from the database, recorded on the day of study, or obtained from the weather service included: horse name, horse age, horse sex, trainer, race date, time of race, time of examination, race track, distance, purse, money earned, weight carried, track condition (a categorical variable), penetrometer reading (an objective measure of the track surface), environmental temperature, humidity, rain fall, wind speed and direction, whether the horse finished the race, finishing place, finishing time of the winner, margin or lengths finished behind the winner, speed rating for the race, number of horses in the race, days since last race, earnings for this race, lifetime earnings up to this race, lifetime starts up to this race, lifetime wins up to this race, lifetime place finishes up to this race, and lifetime show finishes up to this race.

#### **Data analysis and interpretation:**

The relationship between race performance and EIPH was examined using the following dependent variables as indicators of performance: estimated 1200 m race time, estimated racing speed, distance behind the winner, race earnings, and finish position.<sup>9</sup>

Descriptive statistics were calculated, data summarized and distributions of continuous data evaluated for normality. Data with non-normal distributions were transformed to yield a more normal distribution or categorical variable calculated. Exercise-induced pulmonary haemorrhage was defined as a yes/no variable in two ways: presence or absence of blood (EIPH0) or as grade 1 or less (no) and

grade 2 or greater (yes, EIPH1). The severity of EIPH was treated as an ordinal variable of grades 0-4. The modal value of EIPH severity assigned by the 3 observers was used in analysis.

The available variables (listed above) thought to have affected or predicted a horse's performance were included in the analyses. Previous studies have found that there is considerable co linearity among these variables and this was examined in the current study (Gross et al 1999). Principal component analysis was used to create orthogonal (uncorrelated) scores for the highly correlated variables. Variables included in the principal components analysis were time between start of the race and endoscopic examination, weight carried, starting price, number of starters in the race, race distance, purse, penetrometer reading, and age. Lifetime statistics included in the principal components analysis included number of starts, firsts, seconds or thirds, lifetime earnings, and dates of last start and next-to-last start. These scores were then used in the statistical model to account for the variability explained by the initial variables. Different principal component scores were calculated for analysis of the relationship between EIPH and race performance and for the interaction of EIPH and race distance on performance. The potential association between age and EIPH was controlled for by including age as a categorical variable (2, 3, 4, 5, 6, or  $\geq 7$  years) in the model.

Associations between presence of EIPH0, EIPH1 (yes/no) and severity of EIPH (grade 0-4) and estimated 1200 m race time, estimated racing speed, distance behind winner, and race earnings were examined using multivariable analysis of variance. Race earnings were highly skewed and were normalized by logarithmic transformation with values of 0 assigned a value of \$1. The association between EIPH and winning (yes/no), finishing in the first 3 positions (yes/no) and whether any money was earned was evaluated by multivariate logistic regression using a logistic-binomial model. The relationship between severity of EIPH and race performance was examined by discriminant analysis.

The XXX method for multiple comparisons was used to detect differences between least square means derived from ANOVA models. Odds ratios and 95% confidence intervals (95% CI) were based on likelihood ratio statistics calculated from logistic regression models. The type 1 error rate was 5%. Values are presented as mean (SE) unless stated otherwise.

## **Results**

Tracheobronchoscopic examinations were performed on 744 horses competing in 202 races at 26 race meetings. Horses were from stables of 214 trainers with no trainer contributing more than 41 horses (5.5%, median 2 horses, range 1-41). During the period of study, there were 2396 starts by 1428 horses in flat races at meetings at which horses were examined. Field size was  $11.9 \pm 2.5$  (SD) horses. Overall, 52.1% of horses eligible for participation in the study were examined.

Horses examined ranged in age from 2 to 10 years (median 4). The age distribution of the study sample did not differ significantly ( $P > 0.05$ ) from that of the overall population of horses racing during the study period (Figure 1).



Figure 1. Proportion of horses in the study population (all horses) and in the sample group in each age category.

Three hundred and six females, 375 geldings and 63 intact males were examined and the distribution of sexes in the sample group did not differ ( $P > 0.05$ ) significantly from that of the population of horses available for study (Figure 2). Race distances were 1000 to 3200 meters.

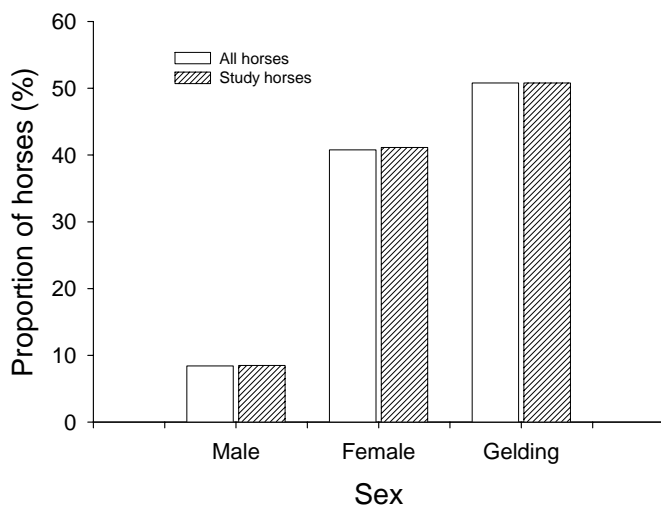


Figure 2. Proportion of horses in the study population (all horses) and in the sample group according to sex.

Fifty four horses (7.3%) finished in first place and 170 (22.9%) finished in the top 3 places. The proportions of horses examined that won ( $P = 0.3$ ) or finished in the top 3 places ( $P = 0.7$ ) were not different to that in the population of horses from which the study sample was drawn.

Endoscopic examinations were performed  $31 \pm 12$  min (SD) after racing. Blood was detected in the airways of 412 (55.3%) horses (Figure 3).



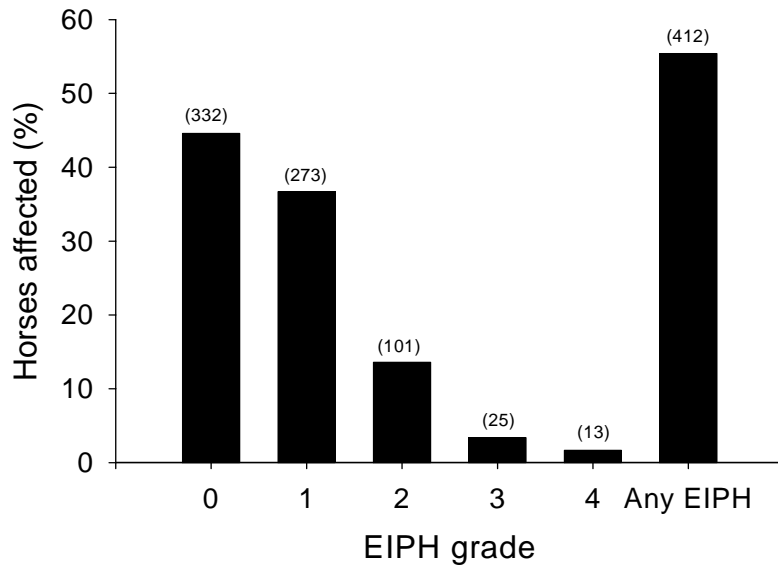


Figure 3. Proportion of horses with EIPH. Numbers above bars refer to actual number of horses.

Horses with  $EIPH \leq 1$  were 4.03 (1.45 to 14.3, 95% confidence interval,  $P = 0.006$ ) times more likely to win and 1.78 (1.05 to 3.07,  $P = 0.03$ ) times more likely to finish in the first 3 positions than were horses with  $EIPH \geq 2$ . However, horses with no evidence of EIPH ( $EIPH = 0$ ) were not more likely to win (1.30, 0.68 to 2.47,  $P = 0.43$ ) nor finish in the first 3 places than were horses with  $EIPH \geq 1$ .

Horses with  $EIPH (\geq 1)$  finished further behind the winner than did unaffected horses ( $4.36 \pm 1.16$  vs  $2.60 \pm 1.07$  m,  $P = 0.002$ ). The distance horses with EIPH finished behind the winner was related to the grade of EIPH, with horses with higher grades finishing significantly ( $P = 0.025$ ) further behind the winner (Figure 4). Post-hoc testing detected a significant difference in distance behind the winner for horses with EIPH grade 2 compared with EIPH grade 0.

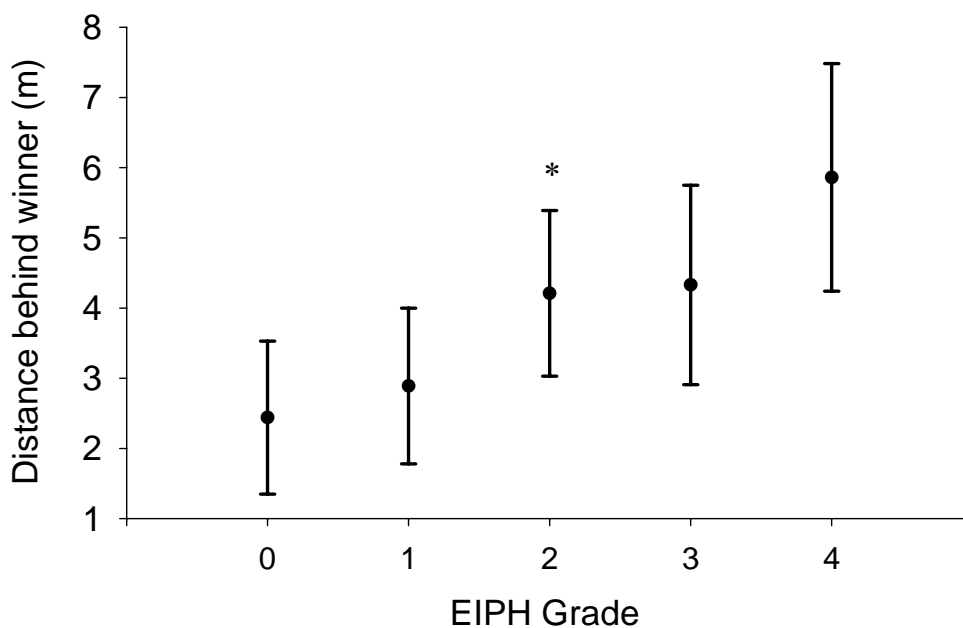


Figure 4. Distance horses finished behind the winner as a function of EIPH grade. Least square mean (SE). \*  $P < 0.05$  vs EIPH 0.

Earnings were significantly associated with EIPH status. While there was not a significant relationship between EIPH status and earnings ( $P = 0.053$ ), horses with  $EIPH \leq 1$  were 3.03 (1.33 to 7.96,  $P = 0.002$ ) times more likely to earn amounts in the top 10% ( $> AUD14300$ ) of money earned.

## Discussion:

The results of this study reveal a consistent association between presence or severity of EIPH and odds of winning or placing, distance finishing behind the winner and likelihood of winning larger purses for thoroughbred horses racing in Victoria, Australia. We conclude that, taken separately or together, these 3 indices of racing success demonstrate that EIPH is associated with impaired performance. The results of this study therefore confirm that EIPH is an important cause of impaired performance in thoroughbred horses racing without premedication with furosemide in Australia.

The association between EIPH and performance has been the subject of a number of studies.<sup>1,5,6,8,10,11</sup> Diagnosis of EIPH has been achieved using either the presence of blood at the nostrils or detection of blood in trachea or mainstem bronchi by tracheobronchoscopic examination.<sup>1,5,6,8,10,11</sup> Use of epistaxis as the sole diagnostic criterion for EIPH is problematic inasmuch as epistaxis is an insensitive indicator of EIPH because many horses with blood in the airways do not have epistaxis. Furthermore, epistaxis is usually only present in horses with the most severe EIPH. Studies using epistaxis as the sole criterion for EIPH therefore underestimate the incidence of EIPH and include only those horses with the most severe form of the disorder. These studies consistently demonstrate an association between epistaxis and impaired racing performance, based on proportion of horses with epistaxis winning or placing.<sup>4,12</sup> However, by not detecting EIPH in the majority of horses these studies do not provide information regarding the effect of lesser degrees of haemorrhage nor of EIPH not associated with epistaxis. Studies relating epistaxis with racing performance therefore provide only limited information regarding the association of EIPH and performance.

Studies of thoroughbred race horses that have relied on tracheobronchoscopic examination for diagnosis of EIPH have not detected an association between EIPH and performance.<sup>1,5,10,11</sup> Reasons for the discrepancy between results of the current and previous studies include differences in study population, study design, and statistical power.

Previous studies of the association of EIPH and performance have examined thoroughbred horses racing in the United States whereas the current study examined only horses racing in one state of Australia. Geographic differences in airway health, racing and training conditions, including track surface, training techniques, and medication use, among other factors, have the potential to affect predisposition to EIPH. Although associations between most of these variables and EIPH have not been demonstrated, and we are not aware of studies documenting a geographic differences in prevalence of EIPH, the possibility of regional differences should be considered when extrapolating results of the current study to other racing jurisdictions.

Importantly, horses in the current study were not premedicated with furosemide before racing, whereas those in other studies, with one exception, raced in jurisdictions that permitted use of furosemide four hours before racing. The effect of furosemide on results of previous studies could have been twofold. Firstly, furosemide administration is associated with superior performance by thoroughbred racehorses.<sup>9</sup> Administration of furosemide to horses with EIPH may have attenuated or ameliorated the detrimental effect of EIPH on performance thus preventing detection of an association of EIPH with impaired performance. Secondly, furosemide may have reduced the severity of EIPH with a consequent improvement in performance. Currently, furosemide has not been demonstrated to reduce the severity of EIPH in horses under competitive racing conditions, although it does reduce the red cell count in bronchoalveolar lavage fluid collected after intense exercise on a treadmill.<sup>13</sup> It is also conceivable that furosemide exerts concurrent and independent effects on both

performance and EIPH. The examination in the current study of horses not premedicated with furosemide may have facilitated detection of an association of EIPH with performance that was not detected in studies of horses administered furosemide.

Previous studies have examined fewer horses than the current study, thereby reducing their ability to detect statistically significant associations between EIPH and performance. The statistical power of the current study was enhanced by the use of analytical techniques that account for the effect of confounding and co linearity among independent variables. Furthermore, previous studies examined only race placing as an indicator of performance, whereas the current study examined race placing, money earned and distance behind winner. The larger number of horses examined in the current study, use of additional indicators of performance and adjustment for confounding factors may have enabled detection of an association of EIPH with performance that other studies were unable to detect.

Cross-sectional studies, such as the current study and others that have investigated the association of EIPH with performance, are susceptible to selection bias unless careful attention is paid to recruitment of subjects. Furthermore, the validity of the study is enhanced if the study sample is shown to be representative of the population from which it is drawn. Whereas previous studies have studied a convenience sample based on race placing,<sup>1</sup> or have not provided criteria used to include horses in the sample group,<sup>5,8,11</sup> the current study used vigorous efforts at pre-enrolment that resulted in a sample of horses that was representative of the study population. Furthermore, horses were examined only once, thereby preventing the statistical and analytical problems associated with multiple examinations of the same horse. The representative sample group and efforts to prevent bias in selection of the study group increase the likelihood that results of the current study can be extended to the larger population of race horses.

The current study did not investigate mechanisms underlying the association of EIPH with performance. Horses with EIPH have lower arterial oxygen tensions during exercise on a treadmill.<sup>14</sup> Instillation of blood into the airways of horses alters respiratory function at rest and reduces the maximal rate of oxygen consumption during exercise on a treadmill. However, the effect of blood instillation on oxygen consumption and respiratory function appears to be related to the volume of blood instilled, with the effect being detectable during exercise only for larger amounts of blood.<sup>b</sup> This finding could explain our observation of an association between severity of EIPH and impaired performance. The impairment of respiratory function induced by blood instillation into the airways and reduction in maximal rate of oxygen consumption may explain the association of EIPH with performance detected in the current study.

We conclude that EIPH is associated with impaired performance by thoroughbred horses racing without premedication with furosemide in Australia. The association between EIPH and impaired performance was apparent as a reduction in the likelihood of affected horses winning or placing, an increase in the distance of affected horses behind the winner, and a decreased likelihood of affected horses winning larger purses. While these indicators of performance are all correlated, they do provide diverse indicators of an association of EIPH with impaired performance. Furthermore, there is an apparent dose-response relationship of severity of EIPH and impaired performance evidenced by the association of severity of EIPH and distance the horse finished behind the winner.

a. Model CF-100TL (1.7 m, 1.1 cm) endoscope, Shirakawa Olympus Co., Ltd., Japan

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### **3. Discussion of results:**

The results of this study are discussed in detail in chapters 1 and 2. The essence of the study is that EIPH is associated with poor performance and that this association with poor performance is detectable using several measures of performance.

### **4. Implications:**

EIPH should be considered as a cause of poor performance in thoroughbred race horses. Given that EIPH is a common condition (~56 % of horses in the current study were affected to some degree) and that it is associated with poor performance, attention should be paid to developing and investigating methods of decreasing the incidence and severity of the condition and reducing the adverse effects of pulmonary haemorrhage. It should be recognized that none of the many proposed treatments currently used throughout the world have been demonstrated to reduce the severity or incidence of EIPH in race horses.