Chapter 1 Exercise-induced pulmonary haemorrhage: An introduction

Exercise-induced pulmonary haemorrhage (EIPH) is a worldwide phenomenon in horses undergoing intense exercise, negatively affecting their health and performance. Most strenuously-exercised horses may be affected, although few will die as a direct result of EIPH. Exercise-induced pulmonary haemorrhage seems to be a physiological response to exercise in racehorses.

"Many horses, especially young horses, are oft the subject to this bleeding at the nose…it proceedeth from much abundance of blood, or that vein which endeth in that place [referring to the head] is either broken, fretted or opened"[83]

1.1 EPIDEMIOLOGY

"But broke a blood vessel and was beaten off"[83]

This was one of the first accounts of epistaxis recorded of Herod, a famous English Thoroughbred stallion, while racing in the 1766 Great Subscription Purse at York, England. For centuries, reports documenting the presence of blood in the nostrils of horses following intense exercise existed.[18] Using epistaxis (Figure 1.1) as the sole

criteria to identify horses with EIPH, the true prevalence of EIPH in the Thoroughbred racing population was repeatedly underestimated with a reported range of 0.15 to 2.41%.[13,18,42,80,81,98,103]

With the advent of modern technology and the availability of flexible fiberoptic endoscopes to examine the lower respiratory tract (Figure 1.2), estimates of the prevalence of EIPH using tracheobronchoscopy in the post race period have been reported in Thoroughbred racehorses (42 to 75.4%),[10,33,55,75,76,82,88] in Standardbred racehorses (26 to 87%),[10,47,50,75] in racing Quarter Horses (62.3%),[31] and in the racing Appaloosa horse (52.1%).[32] In addition, the prevalence of EIPH has been documented in Chilean Criollo horses (60.8%),[2] draft horses (0%),[14] polo ponies (11.1%),[102] cross-country ponies and mixed-breed horses (10%),[94] mixed-breed endurance horses (0%)[94] and Thoroughbreds competing in steeplechase (66.7%).[94] EIPH is also present in racing camels[3] and greyhounds.[44]

EIPH has also been described in man with reports documenting two athletes that developed shortness of breath, haemoptysis, and pulmonary oedema;[36] six elite athletes had increased red cells and protein concentration in bronchoalveolar lavage (BAL) fluid after extreme exertion;[106] in an apparent healthy man after running a marathon[28] and post-swimming.[104]

It is important to note that the reported prevalence and severity of EIPH may depend on the specific diagnostic modality (presence of epistaxis, use of tracheobronchoscopy,

cytological analysis of a tracheal aspirate or bronchoalveolar lavage), the timing and frequency of the diagnostic intervention (pre- or post-race and how often), intensity of exercise (training *versus* race day), and breed difference. Pertinent epidemiological studies reporting on tracheobronchoscopically-detected EIPH or EIPH-related epistaxis have been summarized in Table 1.1.

1.2 PATHOPHYSIOLOGY

Although EIPH is a ubiquitous condition, the precise aetiopathogenesis is unclear as can be seen from the many hypotheses which have been developed over the past years.

"This condition in racehorses remains an enigma"[49]

1.2.1 Chronic pulmonary disease

Chronic obstructive pulmonary disease (COPD) and emphysema was proposed as an underlying lesion of EIPH,[18] however no association was found between the presence of mucous and mucopurulent exudates in the trachea and EIPH.[16,92] Histopathological data was also dissimilar between EIPH and COPD-affected lung.[38,55]

1.2.2 Inflammatory airway disease

Inflammatory airway disease (IAD) is common in young racehorses, and may be characterized by exercise intolerance, coughing, and mucous in the airway[20,50] with a neutrophilic and lymphocytic BAL cytology.[19,87] Other reports on BAL cytology found a neutrophilic, eosinophilic or mastocytic inflammatory profile.[87,101] IAD and EIPH are frequently diagnosed in racehorses and may be a cause of impaired performance.[50] A report previously found an association between IAD and EIPH in young Thoroughbred racehorses.[64]

1.2.3 Upper airway obstruction

Upper airway obstruction (UAO) may include idiopathic laryngeal hemiplegia (ILH), dorsal displacement of the soft palate (DDSP), epiglottic entrapment, epiglottic hypoplasia, subepiglottic cysts, dorsal pharyngeal collapse, arytenoid chondritis, nasopharyngeal masses and vocal chord collapse. Alveolar transmural pressure is greater in horses with airway obstruction while racing[23,30,37] resulting in greater negative intrapleural and alveolar pressures leading to higher transmural pressure.

1.2.4 Pulmonary hypertension

Pulmonary vascular hypertension[48] and arterial hypertension[38] was reported in horses which suffered epistaxis, however these studies failed to record blood pressure prior to

epistaxis and therefore it was uncertain whether the rise in blood pressure was a precursor to epistaxis.

1.2.5 Parasites and thromboembolism

A parasitic or thomboembolic etiology was suggested as a cause of the lesions in the dorsocaudal lung lobes seen in EIPH-affected horses,[66] however no parasitic lesions or thromboemboli could be identified using histopathology.[55]

1.2.6 Haemostasis

Haemostasis was thought to be abnormal in horses with EIPH; however no defects in the intrinsic and extrinsic coagulation pathways or enhanced fibrinolysis were found in exercising horses or horses with EIPH.[5,38,39] Thrombocytopaenia and decreased clot retraction time was reported in horses with epistaxis[38] while exercise decreased adenosine diphosphate induced platelet aggregation.[6] In horses with EIPH, platelets are less responsive to agonists of platelet aggregation (adenosine diphosphate, collagen, platelet activating factor). Furosemide blocked the reduction in platelet aggregation,[4] enhanced platelet function and eliminated platelet trapping in the lung;[15] however how this relates to EIPH is not known.

1.2.7 Haemorrheologic variables

A survey of 49 racehorses before and after racing showed an increase in post-race red blood cell concentration, haemoglobin concentration and haematocrit, leading the authors to conclude hyperviscosity due to exercise-induced splenic contraction may play a causal role in EIPH.[56] Hyperviscosity and an increase in red blood cell deformability may increase shear rate and contribute to capillary wall failure. However, *in vitro*, the viscosity of equine blood decreases with increasing microvascular shear rate.[24]. Since furosemide (150 to 250 mg) had no appreciable affect on the relationship between haematocrit, shear rate, and blood viscosity,[91] haemoconcentration with associated splenic contraction increased cardiac output and mean blood flow velocity may result in increased shear rate and decrease in blood viscosity.[24] Increases in pulmonary vascular pressures during exercise are unlikely to be related to blood viscosity alterations.[79] The presences of echinocytes (speculated erythrocytes) were thought to cause EIPH.[12] It was suggested that as echinocytes are less deformable than erythrocytes and because echinocytosis occurred after endurance exercise,[11] that echinocytes may aggregate, form a thrombus and increase blood viscosity. No difference in the percentage of circulating echinocytes were reported in EIPH-affected and non-affected horses.[56] In contrast to echinocytes made *in vitro*, chronic furosemide induction of echinocytes *in vivo* (1 mg/kg, intramuscular, q12h, for 4 days) were less rigid, aggregated less, and did not alter blood viscosity at high shear rates.[105]

1.2.8 Capillary wall stress

Increased transmural capillary pressures (difference in pressure between the alveolar and capillary lumen) are generated during exercise which cause stress failure of the pulmonary capillaries.[107] Capillaries may then rupture should the transmural stress exceed the tensile strength of the capillary.[108] The stress failure is associated with reversible disruption of the capillary and alveolar epithelium resulting in haemorrhage into the interstitial and alveolar spaces due to the increased permeability (Figure 1.3).[107]

1.2.8.1 Role of the pulmonary circulation

Labeled microspheres injected into the pulmonary circulation and not into the systemic circulation recovered in BAL fluid of treadmill-exercised horses suggested that the pulmonary circulation may be the source of bleeding.[40] In horses, dramatic increases in pulmonary arterial pressure are associated with strenuous exercise.[9,52] Mean pulmonary arterial pressure is 20 to 25 mmHg at rest and may increase to greater than 90 mmHg during intense exercise due to the large cardiac output. In exercise, pulmonary capillary pressure may increase due to increased left atrial and pulmonary arterial pressure while pleural and alveolar pressures decrease resulting in severe stress to the alveolar wall.[8]

1.2.8.2 Role of the bronchial circulation

The bronchial circulation is associated with haemoptysis in humans.[17] Bronchiolitis, haemosiderophage sequestration, interstitial fibrosis and bronchial arterial neovascularization suggesting the involvement of the bronchial circulation in the aetiology of EIPH was reported,[73] however a direct contribution is lacking.

1.2.9 Small airway disease

Small airway disease may impair respiratory mechanics by decreasing dynamic compliance and increasing respiratory resistance, and may cause airway hyper-responsiveness.[22] Concurrent bronchiolitis[85] is common in EIPH-affected horses[55] and may predispose to bronchoconstriction resulting in a decrease in alveolar pressure during inspiration and capillary rupture.[84] Small airway disease may precede the onset of EIPH through previous studies that showed marked pulmonary bronchial circulation development[67] as confirmed by gross examination[70] and computerized tomography of affected lungs.[69] The small airway disease may be further exacerbated by concurrent viral infection, allergy or air pollution.[21]

1.2.10 Temperature and humidity

During exercise-induced bronchoconstriction, increased airflow may cause greater heat-loss from injured mucosa (in humans, the mucosa is hyperreactive to bronchoconstricting

stimuli) resulting in further bronchoconstriction. Temperature and humidity of inhaled air may be critical in the development of exercise-induced bronchoconstriction.[57] The association of EIPH with ambient temperature and humidity has been made previously.[18,82]

1.2.11 Pre-existing pulmonary inflammation

Pulmonary histopathological studies have demonstrated bronchiolitis in EIPH-affected lung sections[70] indicating that EIPH may be due to pre-existing airway inflammation.[73] Autologous intrapulmonary blood inoculation in horses caused a prolonged local inflammatory reaction (21 days) as assessed by bronchoalveolar leucocyte concentration.[60] This caused decreased dynamic compliance and increased respiratory resistance;[1] and resulted in bronchiolitis, alveolitis and increased vascularised interlobular tissue with increased number of haemosiderophages in air spaces and tissues.[99]

1.2.12 Reactive oxygen species

Reactive oxygen species (ROS) and oxidant injury may be responsible for the following: pulmonary structural damage, surfactant damage, leucocyte influx, release of vasoconstrictive and inflammatory mediators, and disrupt the synthesis and action of nitric oxide, a potent vasodilator.[63] A causal link between ROS and EIPH has yet to be proven.

1.2.13 Ventilation/perfusion

Despite intravascular pressures greater in the lower lung, there is evidence that preferential redistribution of flow to the dorsocaudal lung lobes during exercise.[7] However, pulmonary vascular scintigrams in horses with EIPH have shown a perfusion deficit in the dorsocaudal lung lobes.[72]

1.2.14 Impact-induced trauma

Through loading of the chest by the forelimbs which produce shear forces within the lung that can either cause or worsen EIPH, locomotory impact-induced trauma was proposed as the underlying cause of EIPH.[89,90] This theory proposed that following locomotory impact of the forelimb, a pressure wave is generated which passes from the scapula, through the body wall, to the dorsocaudal lung lobes causing tissue disruption which may lead to EIPH.[90] Interestingly, a recent report found that horses undertaking steeplechase races were at increased risk of epistaxis compared to horses competing in flat racing further suggesting impact-induced trauma may play a role in EIPH.[65] However, there is no evidence to support a locomotor-induced intrapulmonary or intrapleural pressure wave.[41]

1.3 PATHOLOGY

Bilaterally symmetrical discolouration of the dorsocaudal regions of the caudal lung lobes with associated partial small airway obstruction, increased tissue compliance and direct involvement of the bronchial arterial circulation were reported in a study of 26 Thoroughbred horses with confirmed EIPH.[67] Previous autopsy reports on horses suffering EIPH have included: pleural tears with thoracic haemorrhage and epistaxis,[93] massive pulmonary tissue haemorrhage,[80,83,100] and haemosiderophages.[100]

1.4 CLINICAL SIGNS

1.4.1 History

Frequently, racehorses with EIPH may suffer poor performance, or less commonly epistaxis. Depending on the volume of blood present in the trachea, unilateral or bilateral epistaxis may be noticed at the end of the race, in the parade ring, or on return to the paddock when the head is lowered. Epistaxis may be repeatable event following strenuous exercise.

1.4.2 Physical examination

No definitive set of clinical signs exists which can readily be used to diagnose EIPH. Affected horses may be anxious, cough and swallow frequently.[75,76] Coughing and

tracheal crackles may be non-specific for blood in the airway; however swallowing may be a more consistent sign. Swallowing may be initiated by blood pooling in the larynx and pharynx due to the mucociliary escalator clearing blood from the lower respiratory tract. Although infrequent, dyspnoea may be seen in the most severe forms of EIPH due to hypoxia caused by massive bleeding into the airway. Dyspnoea may also occur due to pulmonary abscess rupture, haemothorax, pneumonia or pneumothorax. Epistaxis may occur in a minority of racehorses following strenuous exercise.

1.5 DIAGNOSIS

1.5.1 Epistaxis

In the past, horses were classified positive for EIPH if blood was seen from one or both nostrils. Such horses are frequently referred to as "bleeders". A diagnosis of EIPH based solely on the presence or absence of epistaxis should be actively discouraged as its use as sole criteria for estimating the prevalence of EIPH is inaccurate. Epistaxis is an insensitive indicator of EIPH, occurring in only the most severely affected horse and may also be non-specific for pulmonary haemorrhage. Therefore, the identification of horses with EIPH by the presence of epistaxis will grossly underestimate the prevalence of EIPH by allowing for inclusion into a study of only the most severely affected horses. Obviously, horses affected to lesser degrees, are not included in such analyses, thereby providing limited information regarding the association of EIPH and performance.

1.5.2 Tracheobronchoscopy

EIPH is definitively diagnosed by post exercise (within 120 minutes of racing) endoscopic examination of the upper respiratory tract and detection of the presence and severity of blood in the trachea. Tracheobronchoscopic assessment of EIPH is a quick, minimally-invasive technique that allows immediate classification of racehorses with EIPH according to a previously established grading system[34] without laborious, time-consuming laboratory processing of samples.

1.5.3 Cytological examination of airway secretions

EIPH may be detected in tracheal aspirates or broncho-alveolar lavage fluid (BALF) that contains red blood cells or macrophages with red blood cells or haemoglobin pigment known as haemosiderophages (Figures 1.4, 1.5 and 1.6).[26,58] Reports exist on BALF findings in normal horses.[25,26] Predominant cell types are macrophages and lymphocytes, and neutrophils (< 10% of cells).[25,26] BAL is a common technique and can be used to detect EIPH by measuring the concentration of erythrocytes and haemosiderophages.[58] A correlation between the amount of haemorrhage (erythrocyte concentration) and high mean pulmonary arterial pressure was demonstrated[62] while an association between EIPH and exercise intensity was suggested as horses with the highest maximal oxygen consumption have the most erythrocytes in the BALF.[59] Studies have reported using red blood cell counts to quantify EIPH,[27,43,46,62] however its association with the severity of EIPH has not been studied nor has its relationship with tracheobronchoscopic results.

It must be remembered that EIPH does not uniformly affect the lung, so the BALF cytology only evaluates a regional portion of the lung, and regional pulmonary differences may exist in red blood cell or haemosiderophage percentage.

1.5.4 Diagnostic imaging

Thoracic radiography may reveal distinctive changes to the dorsocaudal lung lobe (Figure 1.7 and 1.8). Radiographic changes may include diffuse but localized increase in density which is time-dependant, varying from an alveolar pattern to an interstitial or bronchial pattern.[66] Radiographically discernible increases in interstitial opacity may be related to lesion severity.[71] Lung abscesses may also be identified too.[77] However, many EIPH-affected horses may only have mild or no radiographic signs. Radiolabled red blood cells and scintigraphy have been used unsuccessfully in an attempt to localize and quantify pulmonary haemorrhage. Trans-thoracic ultrasonography may reveal structural changes in the dorsocaudal lung lobe (Figure 1.9).

1.5.5 Autopsy

Typically, post mortem findings may show epistaxis (Figure 1.10) and include petechiation and haemorrhage (acute) (Figure 1.11) to blue/grey or blue/brown discolouration of the visceral pleural surface of the dorsocaudal lung lobes in horses with chronic EIPH.[73] Typically, horses may have died from another cause, and the EIPH-induced lesions are incidentally noticed. Histopathological examinations of affected areas

reveal bronchiolitis, haemosiderophages, peribronchilolar and perivascular fibrosis, as well as fibrosis of the interlobular septa and pleura.[70]

1.6 THERAPEUTIC OPTIONS

1.6.1 High transmural pulmonary capillary pressure

Furosemide (frusemide) is currently used by racing jurisdictions (USA, Canada, Mexico, UAE, and parts of South America) as prophylaxis for EIPH in Thoroughbred, Standardbred and Quarter Horse racing. Although widespread use of furosemide exists, the clinical efficacy of furosemide in horses with EIPH has yet to be determined under natural field conditions. During exercise, high transmural capillary pressures cause stress failure of the pulmonary capillaries and subsequent haemorrhage.[106] Dose-dependant decreases in right atrial, pulmonary arterial/wedge/capillary pressures have been reported using furosemide in exercising horses.[54] Therefore, by limiting the increase in pulmonary artery and pulmonary capillary pressure of exercising horses, furosemide may reduce the frequency and severity of pulmonary capillary rupture.[52,53] Furosemide decreases the severity of EIPH in Thoroughbred horses exercised on a treadmill,[27,43] however did not have an affect on prevalence of EIPH under natural field conditions.[10,97] Conflicting reports exist regarding the use of furosemide in natural field conditions and its efficacy as evaluated by tracheobronchoscopic examination.[10,78]

A variety of drugs have been used to promote pulmonary vasodilatation in horses with EIPH and have failed to reduce the prevalence of EIPH or have an affect on pulmonary artery pressure: antihypertensive drugs (guanabenz and clonidine), angiotensin-converting enzyme inhibitors (enalopril), phophodiesterase inhibitors (sildenafil, aminophylline and pentoxifylline), and nitric oxide donors/analogs (nitroglycerin, nitroprusside and L-arginine).

1.6.2 Upper airway obstruction

UAO may increase alveolar transmural pressure in race horses resulting in greater negative intrapleural and alveolar pressures leading to higher transmural capillary pressure.[23,30,37] Although unproven, there may be an association between UAO and severity of EIPH. The use of nasal dilator bands (Flair® strips) reduced red blood cell counts in the BALF of intensely-exercised horses[27,43] by dilating the nasal valve and causing a reduction in nasal resistance.[35]

1.6.3 Lower airway obstruction

Horses with EIPH may have concurrent bronchiolitis[85] predisposing to bronchoconstriction and resulting in a decrease in alveolar pressure during inspiration and capillary rupture.[84] Although the exact role of small airway disease in EIPH is unclear, therapy is aimed at reliving inflammation and bronchoconstriction. The efficacy of beta-adrenergic bronchodilatory drugs (clenbuterol and albuterol) is still unclear in

preventing EIPH. An inhaled parasympatholytic drug (ipratropium) helped prevent EIPH in two horses.[96] Also the use of corticosteroids (dexamathasone, fluticasone and beclamathasone) and cromolyn sodium have not been demonstrated to prevent EIPH. Other therapies that have been unsuccessful in treatment of EIPH include inhaled water vapor and low allergenic stall bedding.

1.6.4 Interstitial inflammation and bronchial angiogenesis

Intrapulmonary blood accumulation results in alveolar fibrosis and bronchial artery angiogenesis.[60,61,68] Therefore treatments (such as corticosteroids) have been proposed to stop inflammation and decrease fibrotic damage. Certain racing jurisdictions maintain and enforce rest periods for horses displaying epistaxis, however how rest affects EIPH in the short or long term is unknown.

1.6.5 Haemostatic dysfunction

Neither defective intrinsic and extrinsic coagulation pathways nor enhanced fibrinolysis was found in horses with EIPH.[5,38,39] Despite an intact coagulation cascade, aminocaproic acid (inhibitor of fibrin degradation), estrogens and vitamin K have been used to prevent EIPH unsuccessfully.

The use of aspirin has been advocated due to increased platelet aggregation possibly contributing to EIPH;[51] however, aspirin inhibits platelet aggregation and prolongs coagulation time.[45]

Bioflavinoids have been used to decrease capillary fragility and stop bleeding; however there was no demonstrable efficacy in the use of hesperidin and citrus bioflavinoids.[95] Similarly, vitamin C has no proven benefit in EIPH.

1.7 RISK FACTORS

The prevalence of EIPH is affected by age, and speed. EIPH occurs more often in older horses[55,76,80,82] and with increasing speed.[74,82] Racing rather than breezing in Thoroughbred racehorses was associated with a higher prevalence of EIPH, while EIPH lesions were not seen in young Thoroughbred racehorses that were trained at speeds less than 7 meters per second.[74,82] The effect of sex on the prevalence of EIPH has not been consistently reported.[55,76,80,82,92]

1.8 EFFECT ON RACE PERFORMANCE

"[Herod's] form at times was unaccountably bad and it is significant that the first and only time he met a number of runners he showed the weakness [bleeding]"[83]

This was one of the earliest reports linking bleeding episodes with poor performance.[83] EIPH commonly occurs in racehorses throughout the world, and should only be considered the sole reason for poor performance if severe haemorrhage is present. Cytological examination of tracheobronchial aspirates and BALF may show evidence of EIPH or blood may be detected during tracheobronchoscopy in many under-performing racehorses. Epistaxis is associated with more severe forms of EIPH which cause poor performance and can be fatal.[29,42] Following tracheobronchoscopic evaluation, no relationship between EIPH and finish position was found in a group of 191 Thoroughbred racehorses that finished in first, second and third place,[76] nor in a another group of 98 racehorses.[76] Also, no relationship was proven between EIPH and finish position in 191 racehorses,[82] and between EIPH and performance in 258 Thoroughbred and 296 Standardbred race horses that finished in the top three places.[10] In contrast to the above mentioned reports, 43.9% of Thoroughbred racehorses that finished in the first 3 places had less severe tracheobronchoscopic evidence of EIPH than 55.9% that finished in fourth to fourteenth place.[55] Also, a cross-sectional study of Thoroughbred race horses in Victoria, Australia, showed a strong association between the presence and severity of EIPH and poor performance.[33] This study showed that horses with ≤ grade 1 EIPH were 4.03 times more likely to win and 1.78 times more likely to finish in the top three places

than horses with ≥ grade 2 EIPH.[33] Moreover, horses with higher grades of EIPH finished significantly ($P = 0.025$) farther behind the winner.[33]

Reports on a group of 29 and 92 Standardbred race horses show no relationship between EIPH and finish position.[47,92] However, post race tracheobronchoscopic detection of EIPH in a group of 965 Standardbred racehorses revealed that evidence of EIPH was 1.4 times more likely to occur in those racehorses finishing first or second than those race horses finishing in seventh or eighth place.[86]

As previous studies have either reported a positive,[86] negative[29,33,42,83] or no association[10,47,76,82,92] between EIPH and racing performance, it is still unclear what the relationship is between EIPH and racing performance. Moreover, since EIPH occurs commonly in racehorses throughout the world and due to the multifactorial causes of reduced racing performance in Thoroughbred racehorses, caution should exist when attempting to determine an association between EIPH and racing performance.

1.9 FIGURES AND TABLES

Figure 1.1 Epistaxis in a Thoroughbred racehorse.

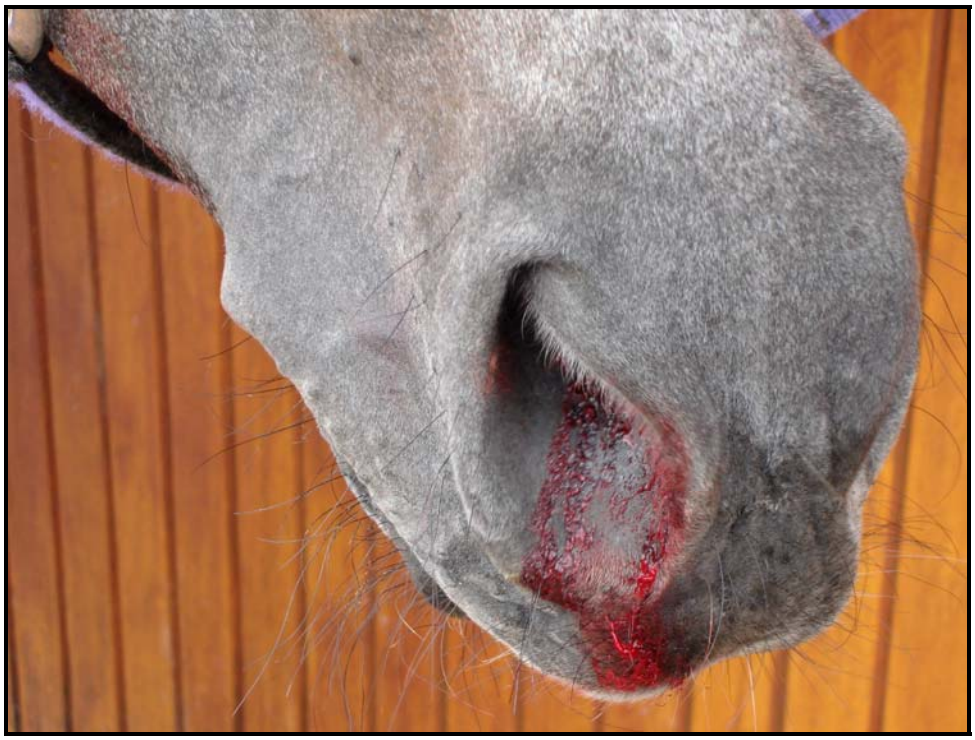


Figure 1.2 Tracheobronchoscopy in a Thoroughbred racehorse.

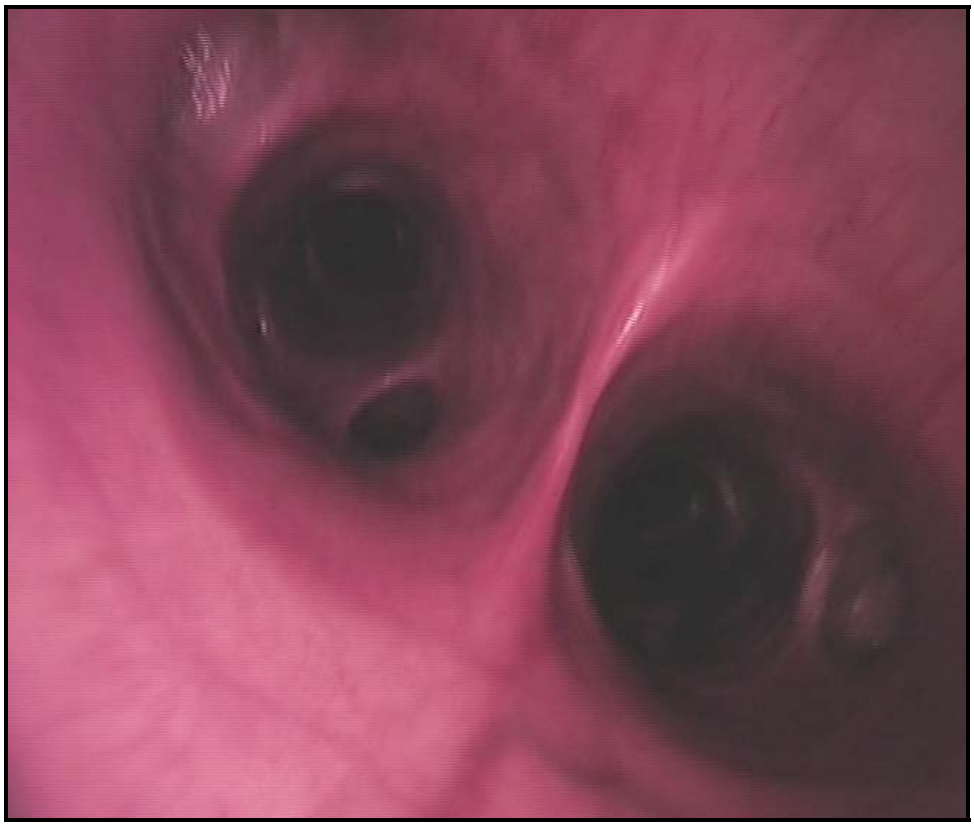


Figure 1.3 Schematic of the proposed mechanism of exercise-induced pulmonary haemorrhage with varying exercise intensity.

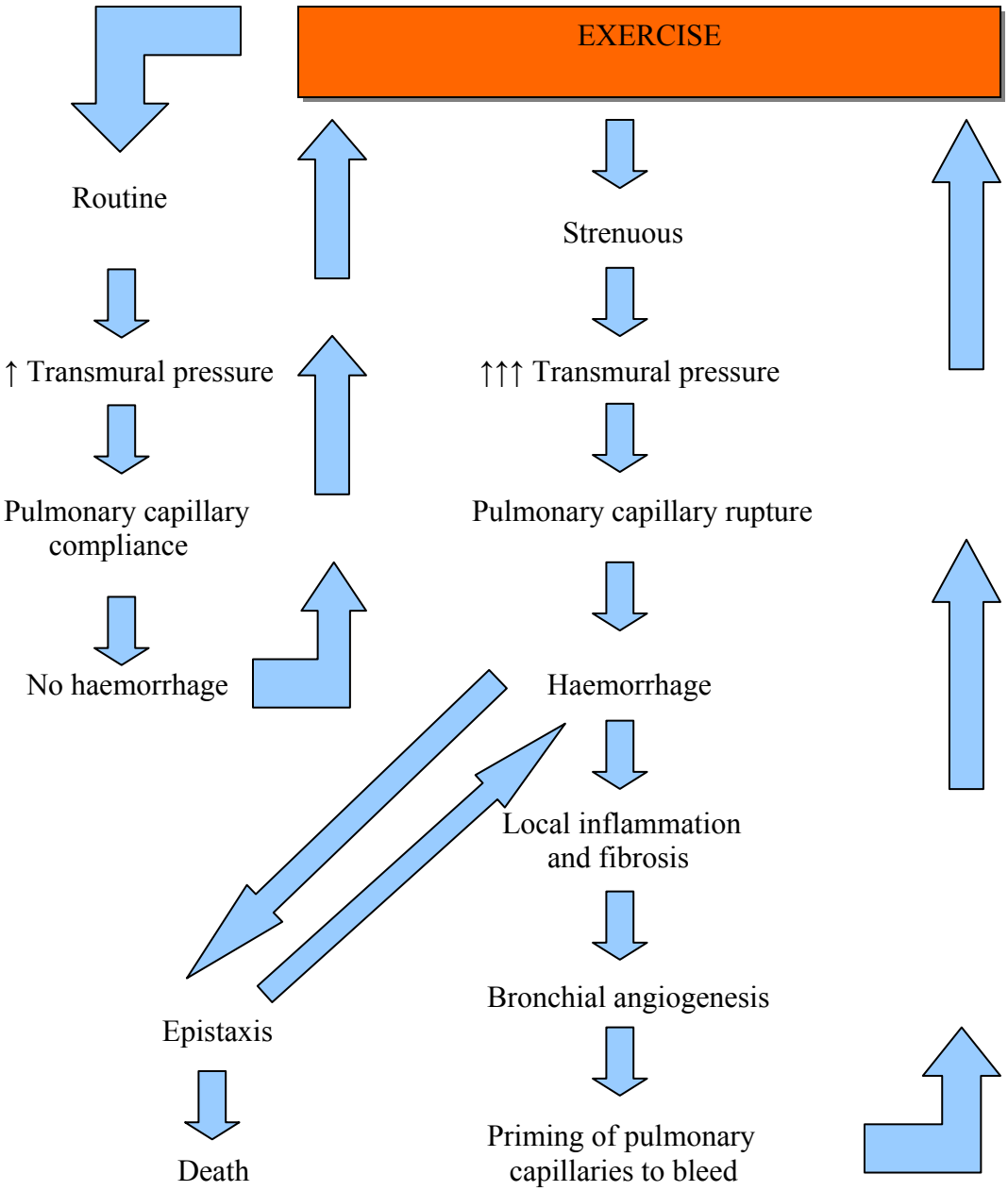


Figure 1.4 Collection of bronchoalveolar lavage fluid from a racehorse.

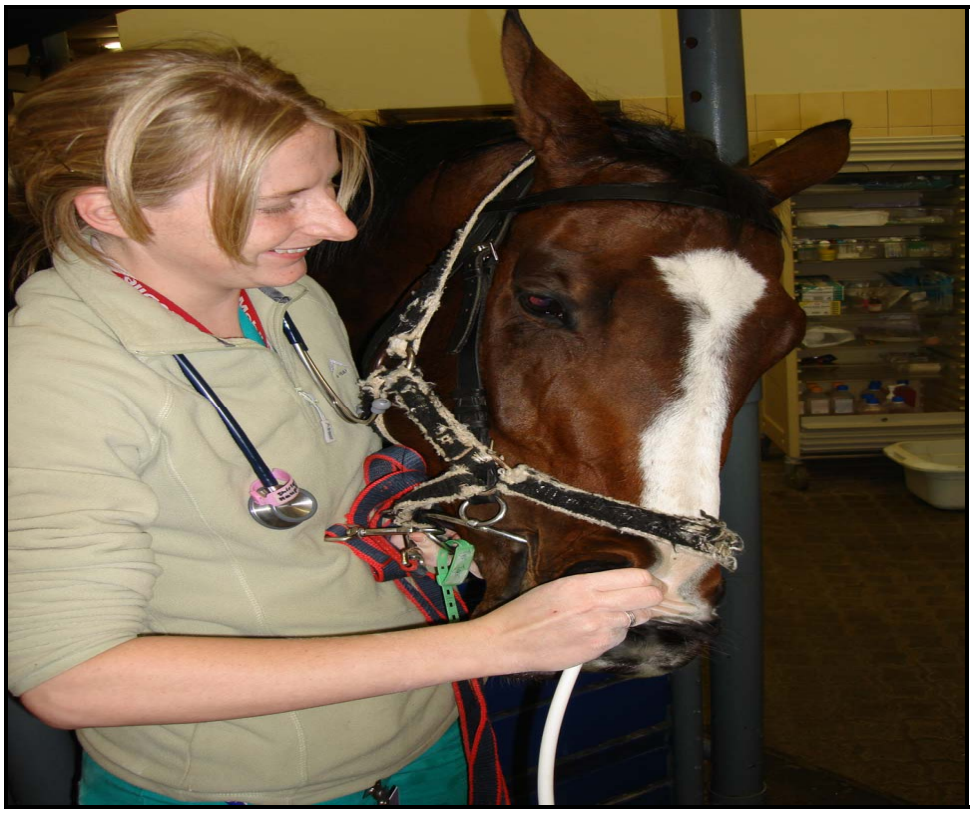


Figure 1.5 Red-tinged bronchoalveolar lavage fluid collected from a racehorse with exercise-induced pulmonary haemorrhage.

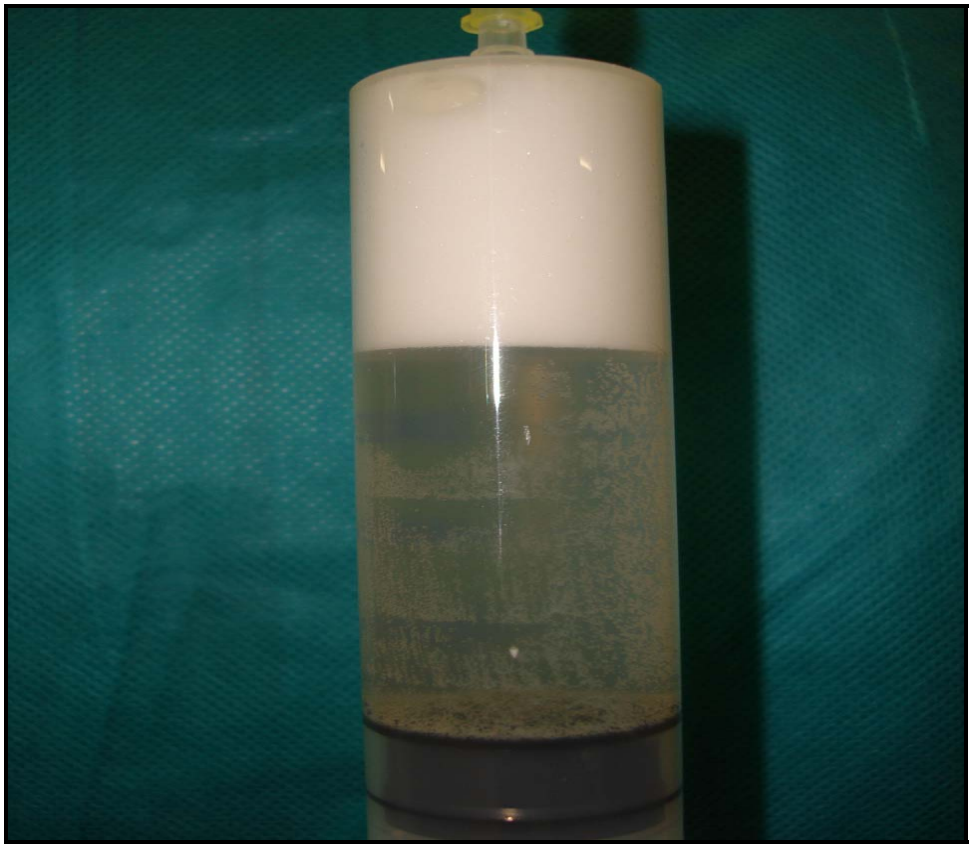


Figure 1.6 Cytological analysis of bronchoalveolar lavage fluid from a racehorse with exercise-induced pulmonary haemorrhage reveals numerous haemosiderophages.

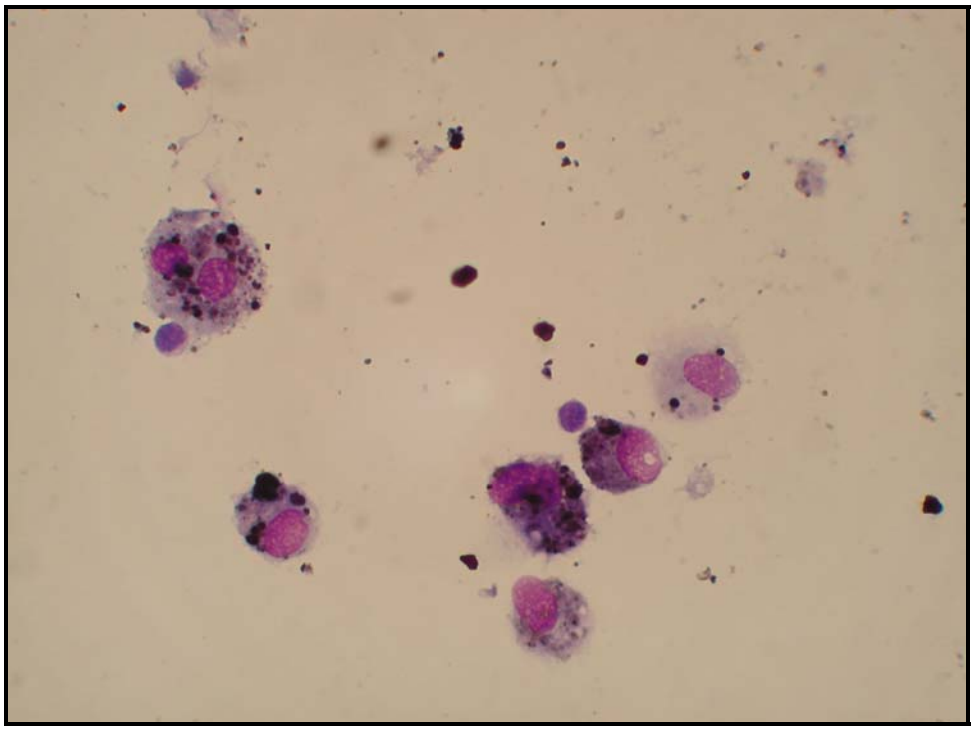


Figure 1.7 A three-year old Thoroughbred filly with a history of epistaxis after strenuous exercise. There is a mixed interstitial and alveolar infiltrate in the caudodorsal lung lobe suggestive of pulmonary haemorrhage.

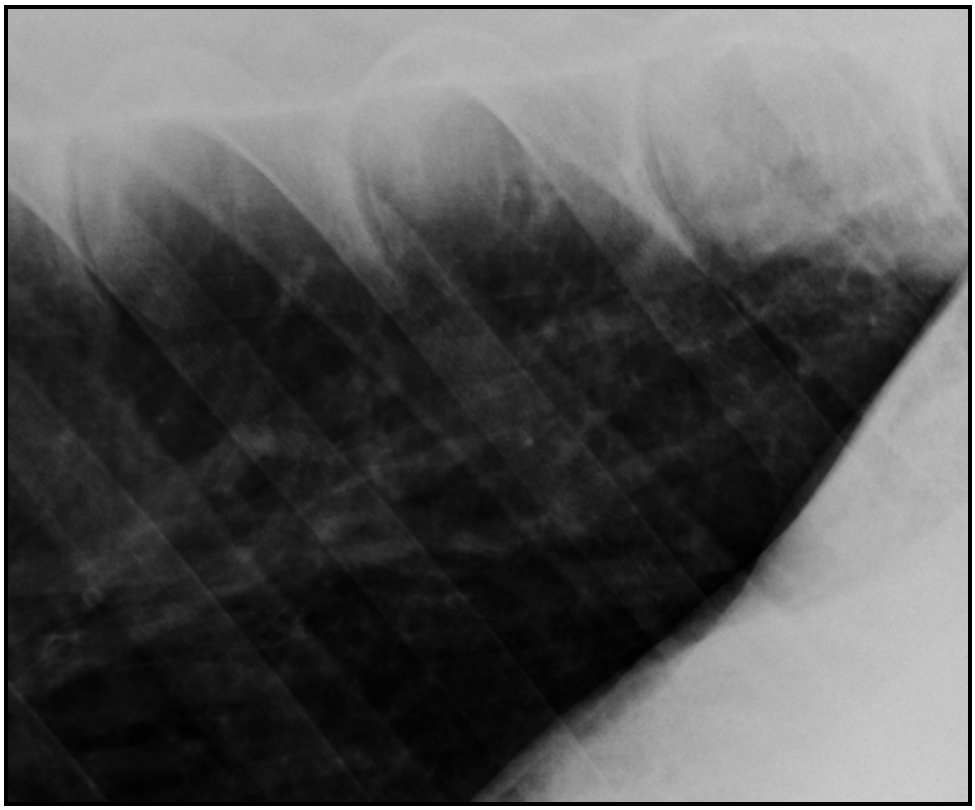
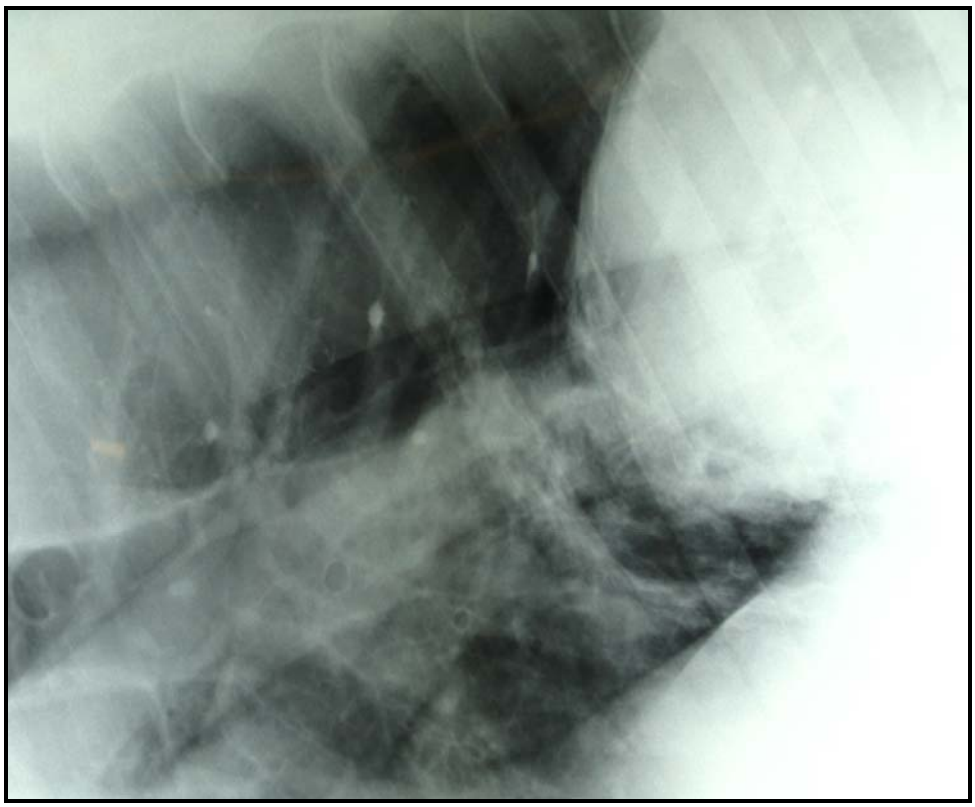


Figure 1.8 Dorsocaudal view of the thorax of a seven year-old Standardbred pacer with a history of poor performance, frequent coughing and pyrexia. Note the well demarcated, round mass consistent with a pulmonary abscess in the dorsocaudal lung lobe.



Courtesy of Dr. Alexa Burton, Large Animal Internal Medicine, Cornell University, USA.

Figure 1.9 Sonogram of the right, dorsocaudal hemithorax in the 17th intercostal space obtained from a three year old Thoroughbred filly with a history of epistaxis after strenuous exercise. Note the dimpling of the visceral pleural surface and comet-tail artifacts originating from the lung.

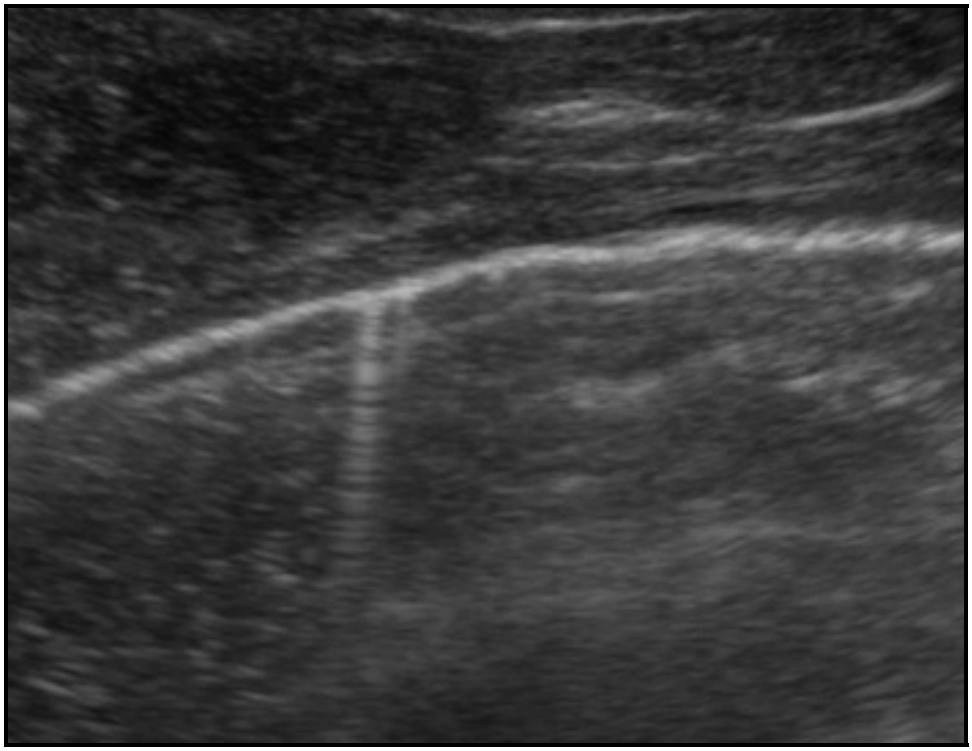


Figure 1.10 Acute death due to exercise-induced pulmonary haemorrhage in a Thoroughbred racehorse: note the mucous and blood present at both nares.

Courtesy of Dr. June Williams, Section of Pathology, Onderstepoort, University of Pretoria.

Figure 1.11 Acute death due to exercise-induced pulmonary haemorrhage in a Thoroughbred racehorse: note the massive pulmonary haemorrhage and blood pooling in the trachea.

Courtesy of Dr. June Williams, Section of Pathology, Onderstepoort, University of Pretoria.

Table 1.1 Epidemiological studies of exercise-induced pulmonary haemorrhage.

Study and Reference Number	Year	Study Size	Breed	Study Location	EIPH Prevalence	Epistaxis Prevalence	Diagnostic Modality
Pfaff, G. (80)	1950	4015	TB	South Africa	NR	1.2%	Epistaxis
Bourke, J.M. (13)	1973	NR	TB	Australia	NR	0.8%	Epistaxis
Cook, W.R. (18)	1974	50	TB	England	NR	0.5 to 2%	Epistaxis
Pfaff, G. (81)	1976	5292	TB	South Africa	NR	2.41%	Epistaxis
Pascoe, J.R. *et al* (75)	1980	1180	TB	USA	42%	3%	Endoscopy
Pascoe, J.R. *et al.* (75)	1980	249	STB	USA	26.5%	12%	Endoscopy
Pascoe, J.R. *et al* (76)	1981	235	TB	USA	43%	0.8%	Endoscopy (100cm)
Raphel, C.F. *et al* (82)	1982	191	TB	USA	75.4	9%	Endoscopy (140cm)
Mason, D.K. *et al* (55)	1983	485	TB	Hong Kong	62.5%	3.9%	Endoscopy
Hillidge, C.J. *et al* (31)	1984	231	QH	USA	62.3%	8.3%	Endoscopy (110cm)
Hillidge, C.J. *et al* (32)	1985	94	APP	USA	52.1%	4%	Endoscopy (180cm)
MacNamara, B. *et al* (50)	1990	965	STB	USA	26%	0%	Endoscopy
Lapointe, J.M. *et al* (47)	1994	60	STB	Canada	62%	0%	Endoscopy (100cm)
Kim, B. *et al* (42)	1998	61,181	TB	Korea	NR	0.84%	Epistaxis
Takahashi, T. *et al* (98)	2001	247,564	TB	Japan	NR	0.15%	Epistaxis
Williams, R.B. *et al* (109)	2001	222,993	TB	England	NR	0.83%	Epistaxis
Weideman, H. *et al* (103)	2003	51,465	TB	South Africa	NR	0.165%	Epistaxis
Hinchcliff, K.W. *et al* (33)	2005	744	TB	Australia	55.3%	0.8%	Endoscopy (170cm)
Saulez, M.N. *et al* (88)	2006	1014	TB	South Africa	54.5%	0.8%	Endoscopy (160cm)

NR: not recorded
TB: Thoroughbred
STB: Standardbred
QH: Quarter horse
APP: Appaloosa

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Research focus of this thesis

Disorders of the equine respiratory tract occur worldwide with varying frequency. Currently, a lack of reports exists on such disorders within South Africa, despite the large, active population of racehorses. In South Africa, the National Horse Racing Authority strictly enforces drug testing in Thoroughbred racehorses, thereby allowing research to be more accurately conducted on racehorses that have not been administered pharmaceutical agents which may modify athletic performance. By the creation of such an environment, we were able to determine the prevalence and severity of airway disorders and their relationship with athletic performance. The impetus for this research originated with Kenneth W. Hinchcliff, a world-renowned researcher on exercise-induced pulmonary haemorrhage (EIPH) in Thoroughbred racehorses.

Following the introduction (Chapter 1), this thesis reports original research in Thoroughbred racehorses competing in South Africa, detailing the prevalence and severity of EIPH and its relationship with racing performance (Chapter 2), the prevalence of pharyngeal, laryngeal and tracheal disorders and their relationship with performance (Chapter 3), and the inter-observer reliability in the use of endoscopic grading criteria for certain respiratory tract disorders (Chapter 4). This thesis also provides exciting new information on an association between EIPH and inflammation at a molecular level (Chapter 5) and concludes with a general discussion (Chapter 6).