

The inheritance of liability to epistaxis in the southern African Thoroughbred

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ABSTRACT

This study was carried out to estimate the heritability of liability to epistaxis in the southern African Thoroughbred population. Data of all horses that suffered epistaxis while racing in southern Africa and Mauritius from 1986 to 2002 and involving 1252 bleeders were analysed. Pedigree data covering the period 1960–1986 was used as required to calculate the incidence of bleeding amongst ancestors of the post-1986 era. Only pedigrees of horses that raced were included in this study as it was not possible to predict whether non-runners would have bled had they raced. Consequently all non-runners and also those that raced overseas in countries where bleeding occurrence was not recorded, were excluded. The heritability of liability method as described by Falconer (1989) was used to estimate the relative importance of heredity and environment. For the period investigated, the population incidence for epistaxis in southern African horses was 2.1 %. The estimation of heritability of liability showed that 1st-degree relatives had a figure of 55.4 %. Second-degree relatives had a heritability of 41.3 % and 3rd-degree relatives came in at 30.4 %. The heritability of liability shown in this study could be regarded as being at the lower end of the range but could be appreciably higher. The data depict horses that bled almost exclusively on race days, as only a small percentage (~5 %) was reported as having bled during exercise. Accordingly, the full extent of epistaxis amongst racing Thoroughbreds in southern Africa is difficult to gauge. It is clear that epistaxis in the racing Thoroughbred has a strong genetic basis. It is suggested that horses showing frank bleeding from the nostrils after racing or exercise be suspended, and not used for breeding purposes. This should result in relatively fast progress being made towards eradicating this costly scourge of the modern Thoroughbred racehorse.

Key words: bleeding, EIPH, epistaxis, heritability, inheritance, pulmonary haemorrhage, Thoroughbred.

Weideman H, Schoeman S J, Jordaan G F **The inheritance of liability to epistaxis in the southern African Thoroughbred.** *Journal of the South African Veterinary Association* (2004) 75(4): 158–162 (En.). Jockey Club of Southern Africa, Kenilworth Racecourse, Rosmead Avenue, Kenilworth, 7700 South Africa.

INTRODUCTION

Epistaxis is a common disorder that affects many horses all over the world. Authors have discussed this clinical syndrome since the days of Markham, a Turf historian writing in the late 1500s. He noted that many horses, especially young horses, were often seen bleeding at the nose, which was at times profuse and difficult to stop. Epistaxis is almost always exercised-induced and was once thought to be of a nasal origin caused by increased airflow that irritated and ruptured swollen nasal turbinates. During the early 1970s it was suggested that while horses were bleeding from the nostrils, the source of

the blood was the lungs and not the nasal cavity². This was later substantiated when Pascoe *et al.*¹⁰, after examining horses with the fiberoptic endoscope, confirmed that the lung was as the site of haemorrhage. They were also the first to refer to this affliction as 'exercise-induced pulmonary haemorrhage' or (EIPH), linking the readily identifiable features, exercise and lung haemorrhage.

Worldwide, EIPH is of great concern because of the financial implications resulting from decreased performance, suspension of horses from racing, lost training days and the necessity for pre-race medication. This could account for major expenses in most major horse racing countries of the world. There appears to be a consistent pattern of incidence of EIPH around the world despite many differences in environmental factors, including climate, training and management practices, racing surfaces

and types of competition.

A number of hypotheses have been proposed to explain the pathophysiology. Several earlier ones held that either upper airway obstruction or lower airway disease were necessary to induce abnormalities in ventilation and increases in alveolar pressure that would eventually lead to tearing of lung tissue. According to a recent hypothesis, bleeding from the lungs is caused by stress failure and rupture of the capillary bed of the pulmonary circulation due to an increase in blood pressure caused by strenuous exercise¹⁸. This was subsequently confirmed when it was found that a pressure of between 75 and 100 mg Hg was required to cause stress failure of the pulmonary capillaries in horses¹. Another hypothesis is that during locomotion, as the horses' hooves hit the ground, a force (shock) is transmitted through the legs to the chest and then to the rib cage. As a result, pressure waves are transmitted through the lungs, causing a complex pattern of wave interaction within the lung that ultimately leads to haemorrhage. It has also been suggested¹⁴ that when the horse is involved in strenuous exercise, the stomach and intestines could swing into the sides (ribs) and back to the lungs – thus rupturing capillaries within the dorsocaudal part of the lungs.

Several investigations into the non-genetic factors as the cause of epistaxis have been undertaken over the past 25 years, but the primary factors responsible for EIPH have not been identified¹⁶. A variety of findings have been reported. These include a positive relationship between EIPH and age¹⁶, EIPH and the cooler months of the year⁷, EIPH and sex¹² and EIPH as associated with pulmonary haemorrhage and altitude¹⁷. On the other hand similar studies could not establish any relationship between EIPH and sex⁸, EIPH and the distance raced¹⁵, while no association was found between EIPH and trainer or going⁹.

Very few references relating to the inheritance of epistaxis in the horse could be found in the available literature. In 1913, Robertson¹³, an expert on racehorse pedigrees, went to considerable lengths

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Received: October 2003. Accepted: July 2004.

to prove that the stallions were the prime, if not sole source of epistaxis in the English thoroughbred. He showed the tendency to break blood vessels (bleeding from the nose) is inherited as a simple recessive character. According to him, however, a horse is not likely to break a blood vessel unless he carries the homozygous recessive genes. The 1st report regarding the incidence of epistaxis in a group of racing thoroughbreds was published in South Africa in 1950¹¹. This study found that at least 1.2 % of horses bled from the nose after racing. According to this author, it is claimed that all bleeders trace back to the stallion Herod (foaled in 1758), and that the names of the stallion Hermit (foaled in 1864) and of his grandson Gallinule (foaled in 1884), appear in the pedigrees of many bleeders in South Africa. In the same paper the possibility of a genetic link between epistaxis and heredity is discussed, highlighting Robertson's¹³ findings. In a later publication¹², it is suggested that heredity might be an important factor in the expression of epistaxis, corroborating a statement made that infers that breeding might be a factor influencing the occurrence of epistaxis in racing thoroughbreds².

No research into the mode of inheritance of epistaxis could be found in the literature. After an initial analysis of the data it seemed that a simple Mendelian mode of inheritance should be ruled out (HW, unpubl.). It is thus assumed that it is inherited in a polygenic manner expressing itself as a threshold trait in a categorical way. Epistaxis would appear not to be inherited in a simple manner by a single gene but may have some degree of hereditary basis, demonstrated by a higher incidence among relatives of affected individuals than in the general population.

The calculation of the heritability of liability has been widely applied in the study of the inheritance of human diseases. Estimates obtained for the heritability of liability range from 85 % for schizophrenia to 35 % for congenital heart disease. Knowledge of the heritability is useful in genetic counselling for calculating recurrence risks in families because it allows all the information about a family to be combined correctly.

The increasing prevalence of epistaxis in southern African Thoroughbreds¹⁷ might be an indication that breeders have through selective breeding, developed horses whose lungs can no longer sustain the stress of strenuous exercise. The objective of this study was to estimate the heritability of liability to epistaxis in the South African Thoroughbred population.

MATERIALS AND METHODS

In this study a group of bleeders with a suspected heritable anomaly was selected and their families investigated. The data of all horses that suffered epistaxis while racing in southern Africa and Mauritius from 1986 to 2002 and involving a total of 1252 bleeders were analysed. Owing to cost and time constraints, on-course endoscopy is not employed as a routine procedure on any of the southern African tracks. Only horses that showed frank bleeding from the nose (epistaxis) were recorded as a bleeder and included in this study. About 13 % of bleeders showed a repeated bout of epistaxis and a further 1 % of all recorded bleeders experienced a 3rd bout and permanent suspension. The Jockey Club of Southern Africa started electronic data capture during the 1986 racing season and pedigree information was available as from that time, while earlier information required to calculate the incidence of bleeding amongst ancestors of the post-1986 era was researched retrospectively to 1960 in order that a complete pedigree data file was available for the period 1960–2002. Only records of animals with full pedigree information were considered. Pedigree depth was, on average, 3–4, but not more than 6 generations.

A large number of southern African racehorses (± 1300) were exported to Mauritius during the 1986–2002 period. These horses all raced in southern Africa before exportation. None were officially recorded as a bleeder at the time of leaving southern Africa. Data acquired from the Mauritian Jockey Club showed that an appreciable number of these imports were recorded as having bled since 1990 and these horses were included in the final data set. Bleeders in Mauritius are, similar to South African practice, recorded and suspended for periods varying from 3 months for 1st-time bleeders to 6 months for repeat bleeders and permanent suspension for 3rd-time bleeders. Only the pedigrees of horses that raced were included in this study as it was not possible to predict whether non-runners would have bled had they raced. This necessitated the exclusion of non-runners as well as all those horses that raced overseas in countries where bleeding occurrence was not known, recorded or substantiated. Accordingly, the data of sires, grandsires and uncles (being almost exclusively imported or having raced overseas) and those imported females that were unraced or raced abroad, were excluded for the purpose of this study. Verifying whether horses qualified as runners was time-consuming, as no easily accessible reference containing all

the required information was available. Every horse was thus scrutinised individually for racing performance, making use of the Jockey Club of Southern Africa's Racing Calendar (South African runners) and web site (<http://www.jockeyclubsa.co.za>), and the Action Racing Online's web site (<http://www.aro.co.za>).

In an effort to illustrate the transmission of epistaxis from generation to generation, postproband segregation analysis was done of a foundation mare after researching all her direct offspring. The mare used in the example was chosen because she is from a very prominent South African family with good numerical representation over the 6 generations researched.

In order to estimate the relative importance of heredity and environment, the heritability of liability method developed by Falconer⁵ and elaborated upon in 1989⁶ was used. This method can be described as a device for converting the information contained in the incidence of bleeding in the general population of racehorses that ran and in the relatives of those bleeders, into an estimate of the correlation between relatives¹⁹. The term 'liability' includes all the causes that make an individual more or less likely to bleed. The genetic analysis in terms of liability are valid only if liability is multifactorial with many causes of variation, all with relatively small effects, and the genetic control is by genes at more than 1 or a few loci. Should a character have an underlying continuity with a threshold, which imposes a discontinuity on the visible expression, and the underlying variable is below this threshold level, the individual has 1 form of the phenotypic expression³, being normal. When it is above the threshold, the individual has the other phenotypic expression, namely affected (bleeder). On a phenotypic level, individuals can thus have only 1 of 2 possible values, which might be designated 0 for normal and 1 for affected. In other words an individual either bleeds or not. Mean/average values between groups of animals/families might differ and would thus vary between 0 and 1, while groups of individuals, however, such as families or the population as a whole, can have any value, in the form of the proportion or percentage of individuals that are affected⁵. This is referred to as the incidence. With liability being normally distributed, then, the unit of liability is its standard deviation r . For genetic analyses, incidences must be converted to mean liabilities. The mean liability is then related to the incidence by the (single tailed) normal deviate x , which is the deviation of the threshold from the mean in standard deviation units of liability. Values of x for

different incidences are then taken from a table⁶ giving the truncated normal distribution for large samples with the proportion of the population with values exceeding the truncation point. Thus, from data consisting of the incidences of bleeding in relatives and the general population, the correlation between relatives in respect of liability can be calculated, and from this the heritability can be estimated.

There were altogether 1252 bleeders whose relatives were analysed. The relatives and degree of relationship between them are given in Table 1. Of these, sire-son, sire-daughter, grandfather and uncle were not used as the bleeder status for imported and unraced horses were not known. Since the liability of individuals cannot be measured, it has to be derived from the mean liabilities of groups of individuals.

RESULTS

The numbers of relatives examined and the numbers affected with epistaxis are shown in Table 2.

The population incidence of epistaxis in southern African horses was 2.1%. The corresponding values of x and i were taken from Appendix Table A in Falconer⁶. The correlations, t , were calculated from the approximate equation:

$$t = \frac{m_p - m_r}{i} = \frac{x_p - x_r}{i},$$

where the p and r refer to the population and the relatives respectively, m is the mean as a deviation from the threshold, x is the normal deviate of the threshold from the mean and i is the mean deviation of affected individuals from the population mean⁶.

For 1st-degree relatives,

$$t = (2.034 - 1.37)/2.40 = 0.277, \text{ and} \\ h^2 = 2t = 0.554.$$

Results for 1st-, 2nd-, and 3rd-degree relatives are given in Table 3.

In order to get a clearer picture as to the transmission of epistaxis from generation to generation, pedigrees of bleeder produce from South African broodmares, extending back over 6 generations, were examined and an example is shown in Fig. 1.

Table 1: Relatives showing the coefficients for different levels of relationship.

1st-degree:	2nd-degree	3rd-degree
0.50	0.25	0.125
Sire-son*	Grandfather*	1st cousins
Sire-daughter*	Grandmother	
Dam-son	Uncles*	
Dam-daughter	Aunts	
Full-brothers	Nephews	
Full-sisters	Nieces	
Full-brother/sister	Grandsons	

*Data excluded as bleeder status for imported and unraced horses were not known.

Table 2: The number of relatives affected with epistaxis according to degree of relationship.

Degree of relationship	r	Affected	Total	$P\%$
1st-degree	0.50	202	2406	8.4
2nd-degree	0.25	251	6845	3.7
3rd-degree	0.125	106	4031	2.6

DISCUSSION

Figure 1 shows that the foundation mare 'A' produced 13 foals in all, namely 6 males and 7 females. Two of the males that both raced in South Africa, were affected, 1 of which produced bleeders while the other did not go to stud. Although none of the 2nd-generation females demonstrated epistaxis, all but 1 of these transmitted this trait to future generations. It would appear that this trait might skip generations and appear even after an absence of 4 generations. Mostly, however, it appears in successive generations or after missing 1 generation. In total, 25 descendants of mare 'A' were affected and this syndrome appears to be genetic.

As the bleeding status of most of those sires whose progeny appear in Fig. 1 (except for those that raced in South Africa) and of most sires used in southern Africa are unknown (being imported), the affected-to-affected mating, (mating bleeder to bleeder) which would be the most efficient way to demonstrate the mode of inheritance, is extremely limited. Presently a small number of stallions that raced in South Africa and were recorded as bleeders, are used at stud. Breeding trails involving these sires could be valuable in reproducing this disorder in

an experimental setting and the mode of inheritance proven through a series of designed matings.

The heritability estimates varied from 55.4 to 30.4%, which indicated that the trait has a strong genetic basis. The estimation of heritability of liability shows that the 1st-degree relatives had a figure of 55.4%, a figure likely to be the most accurate of the 3 levels of relationship, as it most likely has the smallest standard error because the number of affected relatives is greatest and the standard error of t is multiplied by 2 rather than 4 or 8. The 2nd-degree relatives had a heritability of 41.3% and the 3rd-degree relatives a figure of 30.4%. From Table 2, the 3rd-degree relatives had, contrary to expectation, a smaller proportion of total number of relatives (4031) compared to 1st-degree (2406) and 2nd-degree (6845) relatives. This, however, is explained by the fact that most male pedigrees, being imported, had to be excluded from analysis because of insufficient or unrecorded bleeder data; a good proportion of imported fillies never raced or were from unraced dams, or had raced overseas where bleeder data were not available. The most reliable estimate is probably that from 2nd-degree relatives because 1st-degree relatives may have some environmental correlation

Table 3: The heritability of liability in the southern African Thoroughbred population.

	p (%)*	x	i	t	r	h^2 (%)
Population	2.1	2.034	2.40			
Relatives						
1st-degree	8.4	1.412		0.277	(0.50)	55.4
2nd-degree	3.7	1.786		0.103	(0.25)	41.3
3rd-degree	2.6	1.911		0.038	(0.125)	30.4

* p = proportion of population with values exceeding the truncation point T ; x = deviation of T from the mean, in standard deviation units; r = coefficient of relationship between relatives; i = mean deviation of individuals with values exceeding T , in standard deviation units from the population mean.

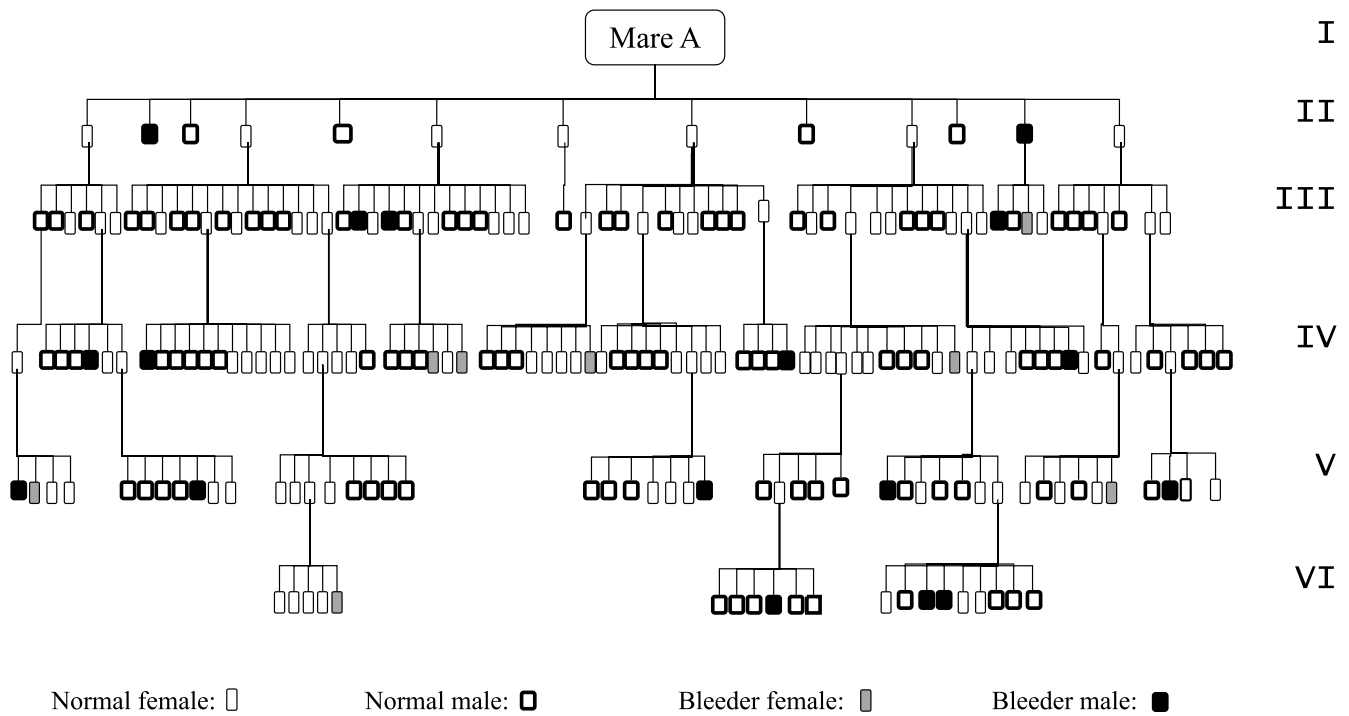


Fig. 1: Genealogy of offspring included in a postproband study of a foundation mare (A), used as an example to illustrate the transmission of epistaxis.

through maternal effects⁵ while 2nd- and 3rd-degree relatives could be very useful in discriminating between different models of inheritance³, but because of the lower degrees of relationship, larger numbers of such relatives will be required, for example to get heritability estimates with low standard errors, and the information on these relatives is often less reliable than on 1st-degree relatives.

The heritability of liability shown in this study could be masked and the full extent not known. This is ascribed to the fact that all officially recorded bleeders are suspended from racing for periods varying from 3 months to permanent suspension. This figure depicts horses that almost exclusively bled on race days, were recorded and suspended after racing by veterinarians licensed by the Jockey Club. A small percentage (about 5% of all recorded bleeders) were reported as having bled during exercise and officially recorded as such. However, it is no secret that a good number of horses bleed during or after exercise while preparing for future engagements and are not reported. The reason for this is obvious, as fearing suspension, only a very small number of horses showing epistaxis during training are actually reported and accordingly the full extent of epistaxis amongst racing thoroughbreds in southern Africa is extremely difficult to gauge. On average about 25–30% of all registered foals never saw the racecourse or had fewer than 5 starts. A good percentage of horses raced very sparingly (1–3 runs only, and others less than would be ex-

pected). This was most probably due to anatomical defects leading to injuries that made it impossible to race or the individual showing no potential as a racehorse and having its career consequently curtailed. A proportion of the racehorse population was thus probably not taxed adequately to establish whether they would have suffered epistaxis had they stayed in training for a longer period of time or had been more intensively trained. Until such time that owners, trainers, jockeys and breeders report all horses stricken with this unfortunate affliction, very slow progress will be made in further identifying the genetic link between epistaxis and breeding.

CONCLUSION

It is clear that epistaxis in the racing Thoroughbred has a strong genetic basis. The increase in the incidence could be curtailed and reduced through genetic selection where relatively fast progress could be made if bleeders were not used for breeding.

In order to eradicate epistaxis, horses showing frank bleeding from the nostrils after racing or exercise should be suspended and not used for breeding purposes. Stricter measures should be enforced to identify bleeders at exercise and training and after racing. Horses should be monitored for at least half an hour or longer after racing to observe whether any signs of external bleeding are obvious. Horses at training or exercise should also be checked for signs of epistaxis in the pull-up area after exercis-

ing and possibly shortly thereafter. Trainers, jockeys and grooms should be advised as to the need to report such horses to the betterment of racing and breeding. If bleeders are not reported, strict measures (fines, suspensions) should be enforced as a preventative measure.

Another alternative, and perhaps a more easily attainable one, would be to 'challenge' sires for bleeding⁴. This would involve testing stallions' offspring in an epistaxis-challenging environment. As a clear positive relationship between racing at sea level and epistaxis was established¹⁷, it might be fruitful to challenge the southern African based sires, comparing all offspring produced that raced at sea level, clearly an unfavourable condition. This may shed more light on the predisposition of imported sires of unknown bleeder status and in some instances racing after treatment with furosemide (Lasix), producing more than their share of offspring that suffer epistaxis.

ACKNOWLEDGEMENTS

The Jockey Club of Southern Africa funded this research. We are grateful to the late Ian Daniels, Data Processing, Jockey Club of Southern Africa, for providing the initial data.

REFERENCES

1. Birks E K, Mathieu-Costello O, Fu Z X, West J 1997 Very high pressures are required to cause stress failure of pulmonary capillaries in Thoroughbred racehorses. *Journal of Applied Physiology* 82: 1584–1592

2. Cook W R 1974 Epistaxis in the racehorse. *Equine Veterinary Journal* 6: 45–58
3. Curnow R N, Smith C 1975 Multifactorial models for familial diseases in man. *Journal of the Royal Statistical Society A* 138(2) 131–169
4. De Greef K H, Janss L L G, Vereijken A L J, Pit R, Gerritsen C L M 2003 Disease-induced variability of genetic correlations: ascites in broilers as a case study *Journal of Animal Science* 79: 1723–1733
5. Falconer D S 1965 The inheritance of liability to certain diseases estimated from the incidence in relatives. *Annals of Human Genetics* 29: 51–76
6. Falconer D S 1989 *Introduction to quantitative genetics*. Longman Scientific & Technical, Essex, England
7. Johnson J H, Garner H E, Hutcheson D P, Merriam J G 1973 Epistaxis. *Proceedings of the Annual Convention of the American Association of Equine Practitioners* 19: 115–121
8. Lapointe J M, Vrins A, McCarvill E 1994 A survey of exercise-induced pulmonary haemorrhage in Quebec Standardbred racehorses. *Equine Veterinary Journal* 26(6): 482–485
9. Mason D K, Collins E A, Watkins K L 1983 Exercise-induced pulmonary hemorrhage in horses. In Snow D H, Persson S G B, Rose R J (Eds) *Equine exercise physiology*. Granta Editions, Cambridge: 57–63
10. Pascoe J R, Ferraro G L, Cannon J H, Arthur R M, Wheat J D 1981 Exercise-induced pulmonary haemorrhage in racing thoroughbreds: a preliminary study. *American Journal of Veterinary Research* 42(5): 703–707
11. Pfaff G 1950 Epistaxis in racehorses. *Journal of the South African Veterinary Association* 21: 74
12. Pfaff G 1976 The incidence of epistaxis in racehorses in South Africa. *Journal of the South African Veterinary Association* 47: 215
13. Robertson J B 1913 Biological searchlight on racehorse breeding: VI. The heredity of blood vessel breaking in the thoroughbred. *Bloodstock Breeders Review* 2: 265–281
14. Schroter R C, Marlin D J, Denny E 1998 Exercise-induced pulmonary haemorrhage (EIPH) in horses results from locomotory impact induced trauma – a novel, unifying concept. *Equine Veterinary Journal* 30: 186–192
15. Speirs V C, van Veenendal J C, Harrison I W, Smyth G B, Anderson G A, Wilson D V, Gilbo B 1982 Pulmonary haemorrhage in standardbred horses after racing. *Australian Veterinary Journal* 59: 38–40
16. Takahashi T, Hiraga A, Kai M, James H 2001 Frequency of and risk factors for epistaxis associated with exercise-induced pulmonary haemorrhage in horses: 251,609 race starts (1992–1997). *Journal of the American Veterinary Medical Association* 218: 1462–1464
17. Weideman H, Schoeman S J, Jordaan G F, Kidd M 2003 Epistaxis related to exercise-induced pulmonary haemorrhage in South African Thoroughbreds. *Journal of the South African Veterinary Association* 74: 127–131
18. West J B, Tyler W S, Birks E K, Mathieu-Costello O 1994 Stress failure of pulmonary capillaries as a mechanism for exercise-induced pulmonary haemorrhage in the horse. *Equine Veterinary Journal* 26: 441–447
19. Wynne-Davies R 1970 The genetics of some common congenital malformations. In Emery A E H (ed.), *Modern trends in human genetics – 1*. Butterworths, London