Received: 21 February 2018 | Accepted: 2 October 2018

DOI: 10.1111/jvim.15350

Journal of Veterinary Internal Medicine Open Access

ACVIM American College of Veterinary Internal Medicine

STANDARD ARTICLE

Management factors and clinical implications of glandular and squamous gastric disease in horses

Benjamin W. Sykes[1,2] | Mark Bowen[3] | Jocelyn L. Habershon-Butcher[3] | Martin Green[3] | Gayle D. Hallowell[3]

[1]School of Veterinary Sciences, The University of Queensland, Gatton, Queensland, Australia

[2]Luoda Pharma, Caringbah, New South Wales, Australia

[3]School of Veterinary Medicine and Science, University of Nottingham, Nottingham, United Kingdom

Correspondence
Benjamin W. Sykes, 51 Fridays Creek Road, Upper Orara, NSW 2450, Australia.
Email: b.sykes@uq.edu.au

Background: To date, risk factors for equine glandular gastric disease (EGGD) have not been described in Thoroughbred racehorses.

Objectives: To determine management factors associated with EGGD, identify clinical signs in affected horses, and compare these to equine squamous gastric disease (ESGD).

Animals: The study was carried out on 109 Thoroughbred racehorses from 8 training yards (3 in the United Kingdom and 5 in Australia).

Methods: Gastroscopic examination alongside a questionnaire regarding management, feeding, exercise, and health.

Results: Management factors and clinical signs were different for EGGD versus ESGD. Exercising ≥5 days per week was associated with a 10.4 times (95% CI [confidence interval]: 1.34-26.9) increased risk of EGGD. Horses racing below expectation were 3.7 times (95% CI: 1.1-16.7) more likely to have EGGD. Trainer was also identified as a risk factor for EGGD. Time in work ≤6 weeks was associated with a decreased risk of ESGD (odds ratio [OR] 0.3; 95% CI: 0.1-0.99). Horses aggressive to humans were less likely to have ESGD (OR 0.12; 95% CI: 0.03-0.54). Horses with stereotypies were more likely to have ESGD (OR 5.0; 95% CI: 1.6-15.9).

Conclusions and Clinical Importance: The findings of our study further support the notion that EGGD should be considered as a distinct disease entity to ESGD. Exercising ≤4 days per week could reduce the risk of EGGD. Horses with EGGD are more likely to perform below expectation and, as such, EGGD might be performance limiting in some affected individuals. Stress minimization could reduce the risk of EGGD.

KEYWORDS

EGUS, risk factors, stomach, ulcer

1 | INTRODUCTION

Gastric disease is a common clinical disorder in racing Thoroughbreds worldwide. The prevalence of equine squamous gastric disease (ESGD) in racing Thoroughbred populations is 66%-91%,[1–3] and this increases when horses are actively racing to 80%-100%.[1,4] There are breed differences with a low prevalence in ponies, moderate prevalence in Warmblood athletes, and higher prevalences in Standardbred and Thoroughbred racehorses.[2,5–7] The prevalence of equine glandular gastric disease (EGGD) has been less well documented until recently. Australian Thoroughbred racehorses have prevalences of between 47%[2] and 65%.[8] To the authors' knowledge, risk factors for EGGD have not been described in Thoroughbred racehorses.

The pathogenesis of ESGD is well described with acid injury to the squamous mucosa, which has limited defense mechanisms and is not normally exposed to a pH of <4, considered the primary factor in disease development. Hydrochloric acid is the dominant factor, but volatile fatty acids produced locally in the stomach associated with

Abbreviations: CI, confidence interval; EGGD, equine squamous gastric disease; ESGD, equine glandular gastric disease; NSAID, nonsteroidal anti-inflammatory drug; OR, odds ratio.

grain feeding are also considered important contributors to disease.[6,9,10] Exercise, and the associated increase in intra-abdominal pressure that results in disruption of gastric pH stratification and "splashing" of highly acidic fluid from the ventral stomach onto the squamous mucosa, is also considered a key factor.[11] A variety of experimental and epidemiological studies have identified risk factors, focused primarily on feeding and exercise practices, for ESGD that influence the management of clinical cases.[6,12–18]

The pathogenesis of EGGD is not known, but it is believed to be caused by the failure of the normal gastric glandular mucosal defense mechanisms.[19] Although there is some evidence that nonsteroidal anti-inflammatory drugs (NSAIDS) administered in excess of the therapeutic dose can cause EGGD in foals and adults,[20] evidence for this occurring under field conditions is lacking.[19] Although bacteria, such as *Helicobacter* spp., have been implicated in the development and perpetuation of glandular disease in other species, they have not been identified in the mucosa of affected horses.[21] As such, the pathogenesis of EGGD remains unknown.

The aims of our study were to determine the management factors that are associated with EGGD, identify clinical signs seen in affected horses, and compare these to ESGD in Thoroughbred racehorses.

2 | METHODS

2.1 | Study design

One hundred and nine Thoroughbred racehorses trained for flat racing from 8 training yards (3 in the United Kingdom and 5 in Australia) were recruited to the study. All horses were in active race training at the time of the examination. In Australia, examinations were performed on every horse maintained at the yard that was in active training, whereas in the United Kingdom, subsets of horses were examined because of sedation drug withdrawal times for racing. The study was approved by the University of Nottingham Ethics and Welfare Committee and conducted under relevant NSW state legislation.

2.2 | Questionnaire survey

A detailed questionnaire was completed for each horse by the trainer to acquire information regarding signalment, management, perceived racing performance, behavior, and general health status. Questions on management factors included training yard location, environment (turnout type and amount, availability of stable toys, and contact with other horses when stabled), feeding (details of forage, concentrate, and supplements), and exercise regime (time in training, frequency, and type of exercise including the use of the horse walker and swimming). Questions on general health status included appetite, body condition and the ease with which body condition could be maintained, other concurrent disease, and any medications administered. Questionnaires were completed by trainers blinded to the gastroscopic findings.

2.3 | Gastroscopic examination and evaluation

Each examination was carried out at the horse's training yard using a portable 3-m video gastroscope. The timing of examinations was variable throughout the weekly training regimen of the horses. All horses were fasted for 6-8 hours before gastroscopy. Access to water was not restricted. The horses were sedated with detomidine (Equimidine, Zoetis, UK; Dozadine, Axon Animal Health, Australia; 10-20 μg/kg bwt iv) with or without butorphanol (Torbugesic, Zoetis, UK; 20 μg/kg bwt iv) and examined for the presence of gastric disease. The squamous, glandular, and pyloric regions were evaluated during the gastroscopic examination, and videos and images were stored of each region from each horse to be reviewed and graded by a single observer (J.L.H.B.). The grades obtained by J. L. Habershon-Butcher using videos and images were used for statistical analysis. The squamous and glandular mucosa were graded separately using a 4-point scale.[22]

2.4 | Data analysis

All data are described and displayed as percentages and 95% confidence intervals (CI), where appropriate. Squamous disease was regarded as clinically relevant if graded ≥2 of 4 in the point scale. Glandular disease was regarded as clinically relevant if graded ≥2 of 4. Univariate analysis to evaluate the relationships between gastric disease, and trainer observations was performed using either chi-square or Fisher's exact tests (if groups less than 5). Variables with a *P*-value <.25 were then considered for inclusion into 2 separate multilevel multivariable logistic regression models that were built using both a stepwise forward and backward elimination procedure.[23] Both models had 3 levels (horse, trainer, and country). The 1st model evaluated the relationship between different types of gastric disease and management factors. The 2nd model concentrated on the relationship between gastric disease and signalment, behavior, and clinical signs. Variables remained in each of the models when fit significantly improved (as assessed by the change in deviance) or if removal resulted in substantial change to the effect of other variables. Effect modification terms were tested among all biologically plausible terms. Where multiple related variables were significant, the most biologically meaningful or the most significant was included in the model.

Significance was assumed at $P < .05$. The 95% CI values displayed used Jeffreys intervals and were calculated using online statistical software (http://epitools.ausvet.com.au/content.php?page=CIProportion). Other statistical analyses were performed using commercial statistical software packages (SPSS 21.0 for Windows, IBM, New York; GraphPad Prism 6.0; GraphPad, California; and MLwiN 2.30, University of Bristol, UK.

3 | RESULTS

There was approximately an equal number of male and female horses with more than two-thirds of the horses being older than 4 years of age. Within the 109 horses evaluated, prevalences of 72% (95% CI: 64%-80%) and 25% (95% CI: 16%-32%) were observed for ESGD and EGGD, respectively.

Signalment and management factors associated with ESGD and EGGD are shown in Table 1. Behavioral factors, stereotypical behavior, and clinical manifestations of disease associated with ESGD and EGGD are shown in Table 2. Results of univariate and multilevel,

TABLE 1 Signalment and management factors associated with equine squamous gastric disease (ESGD) and equine glandular gastric disease (EGGD) in racing Thoroughbreds

Variable	Overall (n = 109) (%) (95% CI)	ESGD ≤1/4 (n = 30) (%) (95% CI)	ESGD ≥2/4 (n = 79) (%) (95% CI)	EGGD ≤1/4 (n = 82) (%) (95% CI)	EGGD ≥2/4 (n = 27) (%) (95% CI)
Gender					
Male	46 (38-56)	53 (36-70)	44 (34-55)	50 (39-61)	37 (21-56)
Female	54 (44-62)	47 (30-64)	56 (45-66)	50 (39-61)	63 (44-79)
Age (y)					
2-3 y	34 (26-43)	40 (24-58)	32 (22-42)	35 (26-46)	30 (15-48)
≥4 y	66 (57-74)	60 (42-76)	68 (58-78)	65 (54-74)	70 (52-85)
Turnout					
No	94 (89-98)	90 (76-97)	96 (90-99)	93 (86-97)	100 (91-100)
Yes	6 (2-11)	10 (3-24)	4 (1-10)	7 (3-14)	0 (0-9)
Bedding					
Shavings	91 (84-95)	90 (76-97)	91 (83-96)	88 (79-94)	100 (91-100)
Other	9 (5-16)	10 (3-24)	9 (4-17)	12 (6-21)	0 (0-9)
Stable toys					
No	84 (77-90)	90 (76-97)	82 (73-89)	87 (78-93)	78 (60-90)
Yes	16 (1-23)	10 (3-24)	18 (11-27)	13 (7-22)	22 (10-40)
Direct contact with other horses					
No	23 (16-31)	30 (16-48)	20 (13-30)	29 (20-40)	4 (0-16)
Yes	77 (69-84)	70 (52-84)	80 (70-87)	71 (60-80)	96 (84-100)
Hay					
No	60 (50-68)	73 (56-87)	54 (43-65)	60 (49-70)	59 (41-76)
Yes	40 (32-50)	27 (13-44)	45 (35-57)	40 (30-51)	41 (24-59)
Haylage					
No	86 (79-92)	80 (63-91)	89 (80-94)	83 (74-90)	96 (84-100)
Yes	14 (8-21)	20 (9-37)	11 (6-20)	17 (10-26)	4 (0-16)
Unprocessed grains					
No	59 (49-68)	60 (42-76)	58 (47-69)	62 (51-72)	48 (30-66)
Yes	41 (32-51)	40 (24-48)	42 (31-53)	38 (28-49)	52 (34-70)
Supplements					
No	17 (11-25)	10 (3-24)	20 (13-30)	17 (10-26)	19 (7-36)
Yes	83 (75-89)	90 (76-97)	80 (70-87)	83 (74-90)	81 (64-93)
Days of exercise per week					
1-4 d	77 (69-84)	87 (71-95)	73 (63-82)	96 (84-100)	72 (62-81)
5-7 d	23 (16-31)	13 (5-29)	27 (18-37)	4 (0-16)	28 (19-38)
Days of fast exercise per week					
1-3 d	78 (70-85)	100 (92-100)	81 (71-88)	78 (68-86)	74 (56-88)
4-7 d	22 (15-30)	0 (0-8)	19 (12-29)	22 (14-32)	26 (12-44)
Swimming					
No	52 (43-62)	60 (42-76)	50 (39-60)	60 (49-70)	30 (15-48)
Yes	48 (38-57)	40 (24-48)	50 (40-61)	40 (30-51)	70 (52-85)
Weeks in work					
<6 wk	7 (3-14)	20 (14-52)	6 (2-13)	11 (6-19)	7 (2-22)
≥6 wk	93 (86-97)	80 (48-86)	94 (87-98)	89 (81-94)	93 (78-98)
Racing to expectation					
No	21 (13-30)	26 (12-44)	19 (11-29)	24 (15-34)	10 (2-28)
Yes	79 (70-83)	74 (56-88)	81 (71-89)	76 (66-85)	90 (72-98)
Medication in last 14 d					
No	86 (79-92)	80 (63-91)	89 (80-94)	82 (72-89)	96 (84-100)
Yes	14 (8-21)	20 (9-37)	11 (6-20)	18 (11-28)	4 (0-16)

TABLE 2 Behavioral factors, stereotypical behavior, and clinical manifestations of disease associated with equine squamous gastric disease (ESGD) and equine glandular gastric disease (EGGD) in racing Thoroughbreds

Variable	Overall (n = 109) (%) (95% CI)	ESGD ≤1/4 (n = 30) (%) (95% CI)	ESGD ≥2/4 (n = 79) (%) (95% CI)	EGGD ≤1/4 (n = 82) (%) (95% CI)	EGGD ≥2/4 (n = 27) (%) (95% CI)
Temperament					
Calm	55 (46-64)	43 (27-61)	61 (50-71)	52 (42-63)	67 (48-82)
Stressed	45 (36-54)	57 (39-73)	39 (29-50)	48 (37-58)	33 (18-52)
Aggression toward people					
No	89 (82-94)	73 (56-87)	95 (88-98)	88 (79-94)	93 (78-98)
Yes	11 (6-18)	27 (13-44)	5 (2-12)	12 (6-21)	7 (2-22)
Anxiety at track					
No	82 (74-88)	73 (56-87)	85 (76-91)	82 (72-89)	81 (64-93)
Yes	18 (12-26)	27 (13-44)	15 (9-24)	18 (11-28)	19 (7-36)
Windsucking					
No	94 (88-97)	90 (76-97)	95 (88-98)	91 (84-96)	100 (91-100)
Yes	6 (3-12)	10 (3-24)	5 (2-12)	9 (4-16)	0 (0-9)
Cribbing					
No	94 (89-98)	100 (92-100)	92 (85-97)	94 (87-98)	96 (84-100)
Yes	6 (2-11)	0 (0-8)	8 (3-15)	6 (2-13)	4 (0-16)
Oral stereotypies					
No	89 (82-94)	100 (92-100)	89 (79-95)	87 (78-93)	96 (84-100)
Yes	13.8 (8-21)	0 (0-8)	11 (5-21)	13 (7-22)	4 (0-16)
Box-walking					
No	90 (83-95)	97 (85-100)	87 (79-93)	88 (79-94)	96 (84-100)
Yes	10 (5-17)	3 (0-15)	13 (7-21)	12 (6-21)	4 (0-16)
Box-kicking					
No	97 (93-99)	100 (92-100)	96 (90-99)	99 (94-100)	93 (78-98)
Yes	3 (1-7)	0 (0-8)	4 (1-10)	1 (0-6)	7 (2-22)
Locomotor stereotypies					
No	88 (81-93)	97 (85-100)	85 (76-91)	88 (79-94)	89 (79-97)
Yes	12 (7-19)	3 (0-15)	15 (9-24)	12 (6-21)	11 (3-27)
All stereotypies					
No	65 (56-74)	83 (67-93)	58 (47-69)	61 (48-73)	78 (60-90)
Yes	35 (26-44)	17 (7-33)	42 (31-53)	39 (27-52)	22 (10-40)
Appetite					
Poor	22 (15-30)	17 (7-33)	24 (16-34)	23 (15-33)	19 (7-36)
Normal	78 (70-85)	83 (67-93)	76 (66-84)	77 (67-85)	81 (64-93)
Body condition					
Thin	16 (10-23)	7 (1-20)	19 (12-29)	15 (8-23)	19 (7-36)
Normal	84 (77-90)	93 (80-99)	81 (71-88)	85 (77-92)	81 (64-93)
Body condition maintenance					
Difficult	16 (10-23)	7 (1-20)	19 (12-29)	15 (8-23)	19 (7-36)
Normal	84 (77-90)	93 (80-99)	81 (71-88)	85 (77-92)	81 (64-93)
Lameness					
No	73 (65-81)	73 (56-87)	73 (63-82)	71 (60-80)	81 (64-93)
Yes	27 (19-35)	27 (13-44)	27 (18-37)	29 (20-40)	19 (7-36)
History of colic					
No	98 (94-100)	100 (92-100)	97 (92-99)	100 (97-100)	93 (78-98)
Yes	2 (0-6)	0 (0-8)	3 (1-8)	0 (0-3)	7 (2-22)
Other disease					
No	95 (90-98)	97 (85-100)	95 (88-98)	98 (97-100)	89 (73-97)
Yes	5 (2-10)	3 (0-15)	5 (2-12)	2 (0-3)	11 (3-27)

multivariable analysis are shown in Tables 3 and 4, respectively. A key finding within the multivariate analysis was that management factors and clinical signs were different for EGGD versus ESGD. Specifically, exercising ≥5 days per week was associated with 10.4 times (95% CI: 1.3-26.9) increased risk of EGGD, when compared with exercising ≤4 days per week, and horses racing below expectation were 3.7 times (95% CI: 1.1-16.7) more likely to have EGGD, when compared with horses racing to, or above, expectation. Trainer was also identified as a risk factor for EGGD. These findings were not present for ESGD.

Time in work ≤6 weeks was associated with a decreased risk of ESGD (OR 0.3; 95% CI: 0.1-0.99). Horses that were aggressive to humans were less likely to have ESGD (OR 0.12; 95% CI: 0.03-0.54). Horses with stereotypies were more likely to have ESGD (OR 5.0; 95% CI: 1.6-15.9). These findings were not present for EGGD.

TABLE 3 Risk factors with associated with equine squamous gastric disease (ESGD) and equine glandular gastric disease (EGGD) in racing Thoroughbreds (univariate analysis)

Variable	Odds ratio (95% CI)	*P*-value
ESGD		
Model 1—Signalment and management factors		
5-7 d per week of exercise (reference, 1-4 d)	2.4 (0.7-7.5)	.20
4-7 d per week of fast exercise (reference, 1-3 d)	1.8 (0.7-4.8)	.21
Model 2—Clinical manifestations		
Stressed temperament (reference, normal)	0.5 (0.2-1.2)	.10
Aggression toward humans (reference, no)	0.15 (0.04-0.5)	.003
Anxiety at racetrack (reference, no)	0.5 (0.2-1.4)	.17
Locomotor stereotypies (reference, none)	5.2 (0.64-42)	.11
All stereotypies (reference, none)	3.6 (1.2-10)	.02
Body condition maintenance (reference, normal)	0.3 (0.07-1.4)	.15
Presence of glandular disease ≥2/4 (reference, ≤1/4)	6.6 (1.5-30.0)	.01
EGGD		
Model 1—Signalment and management factors		
Age 4 y or older (reference, 2-3 y old)	1.8 (0.8-3.3)	.25
5-7 d per week of exercise (reference, 1-4 d)	10 (1.3-79.0)	.007
Racing below expectations (reference, at or above)	3.3 (0.7-15.0)	.15
Receiving any medication in last 14 d (reference, none)	0.17 (0.02-1.4)	.11
Received NSAIDs in the last 14 d (reference, none)	0.16 (0.001-2.9)	.19
Model 2—Clinical manifestations		
Stressed temperament (reference, normal)	0.55 (0.2-1.4)	.19
History of lameness (reference, none)	0.4 (0.19-1.4)	.22
Oral stereotypies (reference, none)	0.25 (0.02-1.5)	.20
All stereotypies (reference, none)	0.45 (0.16-1.2)	.11
Decreased appetite (reference, normal)	1.7 (0.84-4.0)	.20
History of colic (reference, none)	3.3 (0.88-25.0)	.18
Presence of squamous disease ≥2/4 (reference, ≤1/4)	6.3 (2.4-17.0)	.0004

Abbreviation: CI, confidence interval.

TABLE 4 Risk factors significantly with associated with equine squamous gastric disease (ESGD) and equine glandular gastric disease (EGGD) in racing Thoroughbreds (multilevel, multivariable, ordered, proportional odds model)

Variable	Coefficient	SE	Odds ratio (95% CI)	*P*-value
ESGD				
Model 1—Management factors				
Constant	−0.18	0.61		
Time in work <6 wk (reference, ≥6 wk)	1.75	0.78	0.3 (0.1-0.99)	.03
Model 2—Clinical manifestations				
Constant	0.48	0.30		
All stereotypies (reference, none)	1.61	0.59	5.0 (1.6-15.9)	.007
Aggression toward humans (reference, no)	−2.1	0.75	0.12 (0.03-0.54)	.005
EGGD				
Model 1—Management factors				
Constant	−1.9	0.76		
5-7 d per week of exercise (reference, 1-4 d)	2.32	1.1	10.4 (1.34-26.9)	.03
Racing below expectations (reference, at or above)	1.3	0.8	3.7 (1.1-16.7)	.04
Trainer	0.28	0.38		.04
Model 2—Clinical manifestations				
Constant	−2.27	0.68		
Presence of squamous disease ≥2/4 (reference, ≤1/4)	1.31	0.68	4.9 (1.2-19.9)	.04

Abbreviation: CI, confidence interval.

4 | DISCUSSION

The prevalence of ESGD in the present study (72%; 95% CI: 64%-80%) is similar to previous reports,[1,2,12,24] but the prevalence of EGGD (25%; 95% CI: 16%-32%) is lower than previously described in Australian Thoroughbred racehorses (47%-65%).[2,8] The prevalence of ESGD consistently increases as the intensity of management and exercise, and the feeding of high grain diets, increases; however, a similar effect is not consistently observed in EGGD. In endurance horses, the prevalence of EGGD is 16% outside the competition period and 27%-33% during the competition period.[25,26] An abattoir population of feral horses had an EGGD prevalence of 30%, in contrast to an EGGD prevalence of 71% in domesticated horses in the same study.[27] However, relatively high prevalences of EGGD, higher than those observed in the present study, is seen in populations typically considered at relatively low risk of ESGD. Fifty-four percent of leisure horses and 64% sport horses presented for gastroscopic evaluation in the UK had EGGD.[28] Comparably, 72% of Canadian Warmblood show jumpers[29] and 57% of Danish horses used for a variety of purposes[5] had EGGD.

These findings suggest that domestication and management might play a role in EGGD development, but that other risk factors might also be important. To date, the risk factors for EGGD have been poorly described. Breed is a risk factor with Warmblood horses identified to be at increased risk of EGGD.[5,30] This finding potentially explains the relatively high reported prevalences of EGGD in the sport horse populations described above. The reasons behind the discrepancy between the previously described high prevalence in Thoroughbred racehorses,[2,8] and the different findings within a similar population in our study are unclear.

A 10.4-fold increased risk of EGGD was associated with exercising ≥5 days per week in the present study, although no effect of exercise intensity or duration was observed. Exercising Warmblood show jumpers ≥6 days per week increases the risk of disease by 4.6-fold.[29] It has recently been proposed that a relationship between frequency of exercise and gastric blood supply might exist in horses, or that exercise could be an example of physiological stress on the glandular mucosa.[31] Regardless of the pathophysiological link based on the current evidence, it appears that restricting exercise to ≤4-5 days per week could reduce the risk of EGGD.

Trainer was identified as a risk factor for EGGD, and similarly, an increased number of caretakers and riders were identified as possible risk factors in another study looking predominately at riding horses.[30] Horses with EGGD have increased cortisol response to exogenous ACTH administration,[32] and horses with exaggerated response to novel stimuli are also at an increased risk of EGGD.[33] Together, these findings suggest that stress might play a role in the pathogenesis of EGGD, and that stress minimization could be beneficial in reducing the risk of EGGD in some animals. However, the authors acknowledge that specific techniques of stress minimization vary considerably among individuals.

Horses with EGGD were more likely to be racing below expectation than horses without disease. Warmblood show jumpers at international level are less likely to have EGGD than lower level competition horses[29] and polo ponies.[34] These findings suggest that EGGD might have negative impacts on performance. Although not present in our study, poor performance is associated with the presence of ESGD in Thoroughbred racehorses.[12] An alternative explanation is that high-performing horses are better adapted to their environments, and as such, the stress response to their environment is lower than less adapted horses. More experienced show or show jumping horses have lower cortisol concentrations than less experienced horses,[35,36] and if stress, or cortisol, plays a role in the pathogenesis of EGGD as proposed above, a moderated stress response through adaptation could reduce the risk of disease.

Time in work ≥6 weeks was associated with an increased risk of ESGD. This finding is not surprising as acid injury to the squamous mucosa is considered the primary factor in disease development.[19] Increases in carbohydrate intake and exercise associated with increased time in work would be expected to increase the risk of disease given the key roles that both factors play in the pathophysiology of ESGD.[6,9–11]

Stereotypic behavior was seen in animals with ESGD, although not with EGGD. This has previously been reported, although in the previous study it was oral, rather than locomotor stereotypies that were associated with ESGD.[37] Aggression toward handlers was not increased in animals with any form of gastric disease. Animals with ESGD were less likely to display aggressive behavior toward their handlers.

The presence of ESGD was identified as a risk factor for EGGD. This is inconsistent with a previous report[38] but might simply be reflective of the high prevalence of ESGD in the present study population. Alternative possible explanations are that EGGD lesions surrounding the pyloric antrum could result in reduced gastric emptying, making it more likely that the squamous mucosa comes into contact with acidic gastric contents or that some parts of the pathophysiology are shared between these 2 conditions. Further work is needed to understand how these conditions might be linked, but at present, it is the authors' opinion that the body of evidence suggests that they should be regarded as separate disease entities until documented otherwise.

No association was identified between NSAID administration and gastric disease. The authors acknowledge that the study lacked the power to evaluate this particular aspect because of the low numbers of horses receiving this type of medication, but this finding is consistent with current consensus opinions on the subject.[19,31]

There was no association between gastric disease and colic or weight loss in the present study. The failure to associate gastric lesions with colic contrasts results from previous studies.[3,12,39,40] Gastric disease in humans, which by their anatomy are glandular, causes abdominal pain, weight loss, and signs associated with intestinal bleeding.[41,42] Therefore, the failure to associate clinical signs of colic in this population of horses is perplexing, but it could be explained by an absence of pain, a stoic nature of the racehorse in training, or manifestations of pain that are not recognized as colic by trainers. Alternatively, a type II error might be present as the sample size was relatively small for this type of study.

The design and execution of the study has limitations. A large part of the study was questionnaire-based, and it is possible that inaccurate information could have been provided by the trainers. The UK part of the study had potential for bias because the horses used were selected by the trainer to fit in with sedation and withdrawal times for racing. It is possible that trainers provided horses that were performing badly, not eating well, or that they thought the horses had gastric disease, so the prevalence of gastric disease might be overestimated in the UK part of the study. However, the prevalence of ESGD was similar to previous reports, and the questionnaire data did not suggest that the horses examined were underperforming. Furthermore, all horses in the Australian stables were examined, and the Australian horses make up the majority of individuals in the study. As such, selection bias is considered unlikely by the authors. Although the robustness of the grading could have been improved by multiple individuals grading the lesions, the EGUS Council grading system has been widely used and implemented. It has recently been recommended that grading systems not be used for EGGD as they imply linearity for disease.[19] However, the authors used a cutoff of ≥2 of 4 for inclusion in the study analysis with an EGGD lesion ≥2 of 4 in the point scale considered to be where the loss of mucosal integrity has occurred. This is a commonly used therapeutic intervention point for EGGD.[31] Similarly, the authors used ≥2 of 4 for assigning significance to ESGD lesions as this is a commonly used therapeutic intervention point. Lastly, the authors acknowledge that the study could have been

underpowered and thus some important risk factors associated with management might have not been identified.

The potential association between stress and EGGD suggests that further studies evaluating the relationship of stress, stress responses, and EGGD in horses are warranted. Furthermore, studies investigating the potential for limiting the number of days of exercise as a preventative strategy in the management of EGGD appear warranted. Lastly, whether horses benefit from dedicated rest days, or complete rest, during the treatment of EGGD warrants investigation.

In summary, the findings of our study further support the notion that EGGD should be considered as a distinct disease entity to ESGD. Exercising ≤4 days per week could reduce the risk of EGGD. Horses with EGGD are more likely to perform below expectation, and, as such, EGGD might be performance limiting in some affected individuals. Although further work is needed to substantiate this finding, stress appears to play a role in the pathogenesis of EGGD, and management strategies aimed at stress minimization could reduce the risk of EGGD in some individuals.

ACKNOWLEDGMENTS

This work was performed at the Coffs Harbour Racetrack and 5 training yards in the United Kingdom. Preliminary results of this study were presented at the 2012 ACVIM Forum, New Orleans, Louisiana.

CONFLICT OF INTEREST DECLARATION

Authors declare no conflict of interest.

OFF-LABEL ANTIMICROBIAL DECLARATION

Authors declare no off-label use of antimicrobials.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION

The study was approved by the University of Nottingham Ethics and Welfare Committee and conducted under relevant NSW state legislation.

ORCID

Benjamin W. Sykes https://orcid.org/0000-0002-0505-6228

REFERENCES

1. Hammond CJ, Mason DK, Watkins KL. Gastric ulceration in mature thoroughbred horses. *Equine Vet J*. 1986 Jul;18(4):284-287.
2. Begg LM, O'Sullivan CB. The prevalence and distribution of gastric ulceration in 345 racehorses. *Aust Vet J*. 2003 Apr;81(4):199-201.
3. Murray MJ. Gastric ulceration in horses: 91 cases (1987-1990). *J Am Vet Med Assoc*. 1992;201(1):117-120.
4. Murray MJ, Murray CM, Sweeney HJ, et al. Prevalence of gastric lesions in foals without signs of gastric disease: an endoscopic survey. *Equine Vet J*. 1990 Jan;22(1):6-8.
5. Luthersson N, Nielsen KH, Harris P, Parkin TDH. The prevalence and anatomical distribution of equine gastric ulceration syndrome (EGUS) in 201 horses in Denmark. *Equine Vet J*. 2009;41(7):619-624.
6. Luthersson N, Nielsen KH, Harris P, Parkin TDH. Risk factors associated with equine gastric ulceration syndrome (EGUS) in 201 horses in Denmark. *Equine Vet J*. 2009;41(7):625-630.
7. Jonsson H, Egenvall A. Prevalence of gastric ulceration in Swedish Standardbreds in race training. *Equine Vet J*. 2006;38(3):209-213.
8. Sykes BW, Sykes KM, Hallowell GD. A comparison of three doses of omeprazole in the treatment of gastric ulceration in the horse: a randomised, blinded clinical trial. *Equine Vet J*. 2015;47(3):285-290.
9. Frank N, Andrews FM, Elliott SB, Lew J. Effects of dietary oils on the development of gastric ulcers in mares. *Am J Vet Res*. 2005;66(11):2006-2011.
10. Vatistas NJ, Sifferman RL, Holste J. Induction and maintenance of gastric ulceration in horses in simulated race training. *Equine Vet J*. 1999;31(Suppl 29):40-44.
11. Lorenzo-Figueras M, Merritt A. Effects of exercise on gastric volume and pH in the proximal portion of the stomach of horses. *Am J Vet Res*. 2002;63(11):1481-1487.
12. Vatistas NJ, Snyder JR, Carlson G, et al. Cross-sectional study of gastric ulcers of the squamous mucosa in thoroughbred racehorses. *Equine Vet J*. 1999;31(Suppl 29):34-39.
13. Dionne R, Vrins A, Doucet M. Gastric ulcers in Standardbred racehorses: prevalence, lesion description, and risk factors. *J Vet Int Med*. 2003;17(2):218-222.
14. Husted L, Sanchez LC, Olsen SN, et al. Effect of paddock vs. stall housing on 24 hour gastric pH within the proximal and ventral equine stomach. *Equine Vet J*. 2008;40(4):337-341.
15. Husted L, Sanchez LC, Baptiste KE, Olsen SN. Effect of a feed/fast protocol on pH in the proximal equine stomach. *Equine Vet J*. 2009;41(2009):658-662.
16. Nadeau J, Andrews F, Mathew A. Evaluation of diet as a cause of gastric ulcers in horses. *Am J Vet Res*. 2000;61(7):784-790.
17. Bell RJW, Kingston JK, Mogg TD, Perkins NR. The prevalence of gastric ulceration in racehorses in New Zealand. *N Z Vet J*. 2007;55(1):13-18.
18. McClure S, Carithers D, Gross S. Gastric ulcer development in horses in a simulated show or training environment. *J Am Vet Med Assoc*. 2005;227(5):775-777.
19. Sykes BW, Hewetson M, Hepburn RJ, Luthersson N, Tamzali Y. European College of Equine Internal Medicine: consensus statement equine gastric ulcer syndrome (EGUS) in adult horses. *J Vet Int Med*. 2015;29(5):1288-1299.
20. MacAllister CG, Morgan SJ, Borne AT, Pollet RA. Comparison of adverse effects of phenylbutazone, flunixin meglumine, and ketoprofen in horses. *J Am Vet Med Assoc*. 1993;202(1):71-77.
21. Husted L, Jensen TK, Olsen SN, Mølbak L. Examination of equine glandular stomach lesions for bacteria, including Helicobacter spp by fluorescence in situ hybridisation. *BMC Microbiol*. 2010;10:1-8.
22. Andrews F, Bernard W, Byars D, et al. Recommendations for the diagnosis and treatment of equine gastric ulcer syndrome (EGUS). *Equine Vet Educ*. 1999;11(5):262-272.
23. Dohoo I, Martin W, Stryhn H. Model building strategies. In: Pike S, ed. *Epidemiological Research*. Charlottetown, Prince Edward Island: AVC Inc; 2003:317-333.
24. Murray MJ, Eichorn ES. Effects of intermittent feed deprivation, intermittent feed deprivation with ranitidine administration, and stall confinement with ad libitum access to hay on gastric ulceration in horses. *Am J Vet Res*. 1996;57(11):1599-1603.
25. Tamzali Y, Marguet C, Priymenko N, Lyazrhi F. Prevalence of gastric ulcer syndrome in high-level endurance horses. *Equine Vet J*. 2011 Mar;43(2):141-144.
26. Nieto JE, Snyder JR, Beldomenico P, Aleman M, Kerr JW, Spier SJ. Prevalence of gastric ulcers in endurance horses – a preliminary report. *Vet J*. 2004;167(1):33-37.
27. Ward S, Sykes BW, Brown H, Bishop A, Penaluna LA. A comparison of gastric ulcer prevalence in feral and domesticated horses in the UK. *Equine Vet Educ*. 2015;27(12):655-657.
28. Hepburn RJ. Endoscopic examination of the squamous and glandular gastric mucosa in sport and leisure horses: 684 horses (2005-2011) [abstract]. *In: Proceeding 11th International Equine Colic Research Symposium*. Cambridgeshire, UK; 2014:5.

29. Pedersen SK, Cribb AE, Windeyer MC, et al. Risk factors for equine glandular and squamous gastric disease in show jumping Warmbloods. *Equine Vet J*. 2018;50(6):747-751.
30. Mönki J, Hewetson M, Virtala A-MK. Risk factors for equine gastric glandular disease: a case-control study in a Finnish referral hospital population. *J Vet Int Med*. 2016;30(4):1270-1275.
31. Rendle D, Bowen IM, Brazil T, et al. Recommendations for the management of equine glandular gastric disease. *UK-Vet Equine*. 2018;2(1):1-12.
32. Scheidegger MD, Gerber V, Bruckmaier RM, et al. Increased adrenocortical response to adrenocorticotropic hormone (ACTH) in sport horses with equine glandular gastric disease (EGGD). *Vet J*. 2017;228:7-12.
33. Malmkvist J, Poulsen JM, Luthersson N, Palme R, Christensen JW, Søndergaard E. Behaviour and stress responses in horses with gastric ulceration. *Appl Anim Behav Sci*. 2012 Dec;142(3–4):160-167.
34. MacLeod H, Windeyer C, Crosby C, Banse H. Prevalence and risk factors for gastric ulceration in polo horses [abstract]. *J Vet Int Med*. 2015;27(4):1244.
35. Covalesky ME, Russoniello CR, Malinowski K. Effects of show-jumping performance stress on plasma cortisol and lactate concentrations and heart rate and behavior in horses. *J Equine Vet Sci*. 1992;12:244-251.
36. Cayado P, Munoz-Escassi B, Dominguez C, et al. Hormone response to training and competition in athletic horses. *Equine Vet J*. 2006;38(S36):274-278.
37. Lester GD, Robinson I, Secombe C. *Risk factors for gastric ulceration in Thoroughbred racehorses*. Canberra: Australian Government: Rural Industries Research and Development Corporation; 2008:1-42.
38. Murray MJ, Nout YS, Ward DL. Endoscopic findings of the gastric antrum and pylorus in horses: 162 cases (1996-2000). *J Vet Int Med*. 2001;15(4):401-406.
39. Murray MJ, Grodinsky C, Anderson CW, et al. Gastric ulcers in horses: a comparison of endoscopic findings in horses with and without clinical signs. *Equine Vet J*. 1989;21(Suppl 7):68-72.
40. Dukti S, Perkins S, Murphy J, et al. Prevalence of gastric squamous ulceration in horses with abdominal pain. *Equine Vet J*. 2006;38(4):347-349.
41. Tack J, Talley NJ, Camilleri M, et al. Functional gastroduodenal disorders. *Gastroenterology*. 2006;130(5):1466-1479.
42. Armstrong CP, Blower AL. Non-steroidal anti-inflammatory drugs and life threatening complications of peptic ulceration. *Gut*. 1987;28(5):527-532.

How to cite this article: Sykes BW, Bowen M, Habershon-Butcher JL, Green M, Hallowell GD. Management factors and clinical implications of glandular and squamous gastric disease in horses. *J Vet Intern Med*. 2019;33:233–240. https://doi.org/10.1111/jvim.15350