Equine pituitary pars intermedia dysfunction: An international survey of veterinarians' approach to diagnosis, management, and estimated prevalence

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Abstract

The objectives of the present study were to determine if diagnosis and treatment of equine pituitary pars intermedia dysfunction (PPID) vary by geographic region and to report the prevalence of PPID in horses as observed by veterinarians across locations. An online questionnaire was developed for veterinarians who treat horses. Veterinary associations, especially equine specialty subgroups, were contacted and a survey link was sent to members of each organization. Generalized linear models were used to examine whether the method of diagnosis and treatment of this condition, as well as its reported prevalence, differed by geographic region. Veterinarians from 426 separate clinics in 20 countries returned surveys. Diagnosis of PPID varied by region, but was usually based on clinical signs and an adjunct endocrine test. Horses with PPID were treated medically by 63% of veterinarians and 75% of these used pergolide mesylate as treatment. The median prevalence estimated was 1% and this did not differ by geographic location. Half the veterinarians were caring for 5 or more animals with PPID. Overall, diagnostic approach differed in geographic regions. In general, European veterinarians were more likely than those in North America to diagnose PPID based on clinical signs alone, without using an adjunct laboratory test. Veterinarians reported that cost and management responsibilities were their clients' primary concerns associated with the long-term treatment of this disease, which indicates a need for additional treatment options for PPID.

Résumé

Les objectifs de la présente étude étaient de déterminer si le diagnostic et le traitement de la dysfonction de l'hypophyse médiale équine (DHME) varient selon la région géographique et signalent la prévalence de la DHME chez les chevaux, comme l'ont observé les vétérinaires dans différentes localisations. Un questionnaire en ligne a été développé pour les vétérinaires qui traitent les chevaux. Les associations vétérinaires, en particulier les sous-groupes de spécialités équines, ont été contactées et un lien pour un sondage a été envoyé aux membres de chaque organisation. Les modèles linéaires généralisés ont été utilisés pour examiner si la méthode de diagnostic et de traitement de cette condition, ainsi que sa prévalence déclarée, différaient selon la région géographique. Les vétérinaires provenant de 426 cliniques distinctes dans 20 pays ont répondu au sondage. Le diagnostic de DHME variait selon la région, mais était généralement basé sur les signes cliniques et un test endocrinien complémentaire. Les chevaux atteints de DHME ont été traités médicalement par 63 % des vétérinaires et 75 % de ceux-ci utilisaient le mésylate de pergolide comme traitement. La prévalence médiane estimée était de 1 % et cela ne différait pas selon la situation géographique. La moitié des vétérinaires prenaient soin de 5 animaux ou plus avec DHME. Dans l'ensemble, l'approche diagnostique différait selon les régions géographiques. En général, les vétérinaires européens étaient plus susceptibles que ceux en Amérique du Nord de diagnostiquer la DHME en se basant uniquement sur les signes cliniques, sans utiliser un test de laboratoire complémentaire. Les vétérinaires ont signalé que les coûts et les responsabilités en matière de gestion étaient les principales préoccupations de leurs clients liées au traitement à long terme de cette maladie, ce qui indique un besoin d'options de traitement supplémentaires pour DHME.

(Traduit par Docteur Serge Messier)

Introduction

Pituitary pars intermedia dysfunction (PPID), also known as equine Cushing's disease, is a commonly diagnosed endocrinopathy of older horses (1). Clinical signs are typically noted in horses older than 18 y and are rare in horses under 10 y (2–4).

The estimated prevalence of PPID is varied and depends on the age of horses in the referent population, as well as the method used to determine the diagnosis [Table I; (5–15)]. It varies from 0.025% of all horses in a hospital population, to 39% in a study that focused on a small number of aged horses.

The proposed pathophysiology of PPID is a loss of dopaminergic inhibition of melanotrophs in the intermediate lobe of the pituitary gland. The inciting cause is unknown, but oxidative damage to the hypothalamic dopaminergic neuronal soma is thought to play an important role (16,17). The prevalence of Parkinson's disease, a human dopamine-associated neurodegenerative disorder, varies among geographic regions, with higher prevalence in northern and

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Table I. Reported prevalence of equine pituitary pars intermedia dysfunction.

Case Definition	Population (study duration)	N	Age (years)	Location	Prevalence (%)	Reference
Not stated	Practice	4000	All ages	USA	0.075 to 0.15 Estimated	(5)
Hirsutism and endogenous ACTH	Hospital (1 year)	1800	All ages	Netherlands	0.5	(6)
Not stated	Owner questionnaire	1230	All ages	UK	< 1	(7)
Clinical examination and DST	Hospital (4 months)	23	26.5 (median)	UK	39	(8)
Hirsutism or endogenous ACTH or necropsy	Hospital (10 years)	467	All horses > 20 > 30	USA	0.36 10 19	(9)
Veterinarian diagnosed	Owner questionnaire	218	> 20	USA	8	(10)
Shedding/moulting changes "Cushing's syndrome"	Owner questionnaire	918	> 15	UK	12.5 3.3	(11)
Hirsutism DST DST/TRH stimulation	Hospital 11 years 1993 2002	134 632	All ages	USA	0.16 0.025 0.37	(12)
Not stated	Owner questionnaire	797	All ages	UK	2.8	(13)
Hair coat changes	Owner questionnaire	339	> 15	Australia	14	(14)
Endogenous ACTH test	Horses from above study	325	> 15	Australia	21.2	(14)
Not stated	Multi-hospital records 26 years	70 477	All ages	UK	2.9	(15)

agricultural North American states than in southern and industrialized areas (18,19). It is unknown if such a geographic effect exists for equine PPID, whether regional or global.

Domesticated horses are living longer as they are increasingly being managed as companion animals (15). As such, the frequency with which veterinarians are asked to diagnose and manage PPID would be expected to rise. The objectives of this study were to determine whether veterinarians were diagnosing and treating this important chronic disease in a similar fashion across different geographic regions, while also accounting for any differences veterinarians reported in the prevalence of PPID.

Materials and methods

A survey was developed (Supplemental Material A) and pilot-tested with veterinarians experienced in designing and implementing survey tools. The final product was translated into French and Spanish and all 3 versions were managed online for 18 mo (January 2012 to June 2013; Vertical Response, San Francisco, California, USA). Institutional ethics approval was not required because no personal data were requested from respondents.

The survey was brought to the attention of equine practitioners by contacting international colleagues, national and state or provincial veterinary organizations, as well as international equine veterinary groups, including subspecialties of the national associations of individual countries (listed in Supplemental Material B). These groups then notified their respective members through e-mail, digital bulletins, and newsletters. All groups were asked to send a second notification to their membership 6 mo after the initial contact. The authors also distributed paper copies of the survey at the 2012 annual meeting of the American Association of Equine Practitioners in Anaheim, California and completed results were added to the database. All results were compiled using a Windows-based spreadsheet program (Microsoft Excel; Microsoft Canada, Mississauga,

Table II. Number of veterinary responses tabulated by country and grouped by geographic region.

Geographic region	Country	Total number of respondents from each country	Percent of total number	Percent of total number of reported practice country
North America		181	42.5	63
	Canada	83	19.5	28.9
	USA	98	23	34.1
South America		1	0.2	0.3
	Chile	1	0.2	0.3
Europe		73	17.2	25.3
	Belgium	6	1.4	2.1
	Denmark	5	1.2	1.7
	France	3	0.7	1
	Germany	30	7	10.5
	Italy	2	0.5	0.7
	Netherlands	2	0.5	0.7
	Northern Ireland	1	0.2	0.3
	Norway	2	0.5	0.7
	Portugal	2	0.5	0.7
	Spain	6	1.4	2.1
	Sweden	5	1.2	1.7
	United Kingdom	9	2.1	3.1
Middle East		1	0.2	0.3
	Jordan	1	0.2	0.3
Australasia		31	7	10.4
	Australia	23	5.4	8
	Japan	4	0.9	1.4
	New Zealand	3	0.7	1
Africa		1	0.2	0.3
	South Africa	1	0.2	0.3
Reported		287	67.4	100
Unreported		139	32.6	
Total		426	100	

Ontario) and then moved to a commercial statistical package for analysis (SPSS; IBM Canada, Mississauga, Ontario).

Linear regression was used initially to look at differences reported by veterinarians in practice-level prevalence as a percentage (denominator not available) by both practice type and among geographic regions, as these were considered factors that might subsequently impact approaches to diagnosis and treatment. Poisson regression with a log-link function was used to examine the effect of potential risk factors on the number of PPID diagnostic tests used by veterinarians. Logistic regression was used to evaluate potential risk factors for the decision to use a diagnostic test in addition to clinical signs alone; similarly, to determine the potential risk factors behind the decision to use the most common endocrinologic test as opposed to other endocrinologic test options; whether the primary disease, which is assumed to be a functional pituitary tumor, was treated or not; and if the disease was treated with commercial pergolide or compounded pergolide, if available.

All potential risk factors were initially screened using unconditional analysis and variables where P-values of < 0.2 were considered in building the final multivariable model (20). All final models were built using manual-backwards elimination. Variables considered in model building that were not significant and were not mediators were assessed as potential confounders of associations of interest identified during the analytical process. Where 2 or more variables were significant, biologically plausible 2-way interactions were assessed with interactions retained in the final model and reported if the type-3 likelihood ratio test was significant ($P < 0.05$). Differences of $P < 0.05$ were considered significant, and appropriate measures of effect and 95% confidence intervals (CIs) were reported for each analysis.

The number of horses under the care of veterinary practitioners was highly skewed and associations between this variable and the outcomes of interest were not linear. As such, the number of horses under the care of each veterinarian was categorized using cutoff limits based on the 25%, 50%, and 75% data quartiles as follows: 1 to 2 horses, 3 to 4 horses, 5 to 20 horses, and 21 to 250 horses.

Not all questions were answered by all respondents. For other questions, such as country of veterinary practice and practice type,

Table III. Distribution of respondents by practice categories.

Practice category	Number	Overall percentage	Percentage of reported practice categories
Equine only (Specialty)	132	31.0	44.0
Large animal (Equine predominant)	40	9.4	13.3
Large animal (General)	16	3.8	5.3
Combined small animal and equine	47	11.0	15.7
General mixed	65	15.3	21.7
Reported	300	70.4	100.0
Unreported	126	29.6	
Total	426	100.0	

there was only 1 respondent from each of South Africa, Chile, and Jordan. Countries were grouped according to geographic regions (Table II) for analysis and those regions with only 1 respondent were eliminated. For these reasons, not all analyses had the same number of observations included. Specific inclusion criteria and respondent numbers are reported in the appropriate sections of the results.

Results

There were 426 respondents, with 1 veterinarian reporting per clinic. Of these, 404 responded in English, 12 responded in French, and 10 responded in Spanish. Respondents from 20 countries completed the question on practice location (67.4%; 287/426), 34.1% of whom (98/287) were from the US, 28.9% (83/287) were from Canada, and 10.5% (30/287) were from Germany. Countries were grouped into geographic regions as shown in Table II. Practice category varied widely (Table III) and encompassed equine specialists, as well as combined small animal and equine practitioners and general, mixed-animal veterinarians. Most respondents worked in private practice (Table IV).

Of the 426 veterinarians who completed the survey, 360 (84.5%) reported at least 1 horse with PPID in their practice. The median number of horses with PPID under the care of the study respondents was 5 [25% and 75% interquartile range (IQ), 3 to 20]. These animals represented a median of 1.0% (25% and 75% IQ, 0.1 to 5.0) of their equine practice caseload. The median age of affected horses was 20 y (25% and 75% IQ, 18 to 22 y; mean 19.7 +/− 4.3, IQ 9 to 35 y).

Overall, 67.2% (242/360) of veterinarians reported managing PPID horses by treating what was assumed to be a functional pituitary tumor with drugs. Of the remaining 32.8% of respondents (118/360), only 34 explained why they offered no treatment. Of these veterinarians, 79% (27/34) indicated that client limitations prevented them from doing so, while treatment was not warranted in 17% (6/34), and 3% (1/34) were prevented from treating due to lack of availability of drugs. Client limitations were reported as financial (66.7%; $n = 25$) or perceived responsibility of long-term management (33.3%; $n = 14$), with some respondents indicating both as important reasons for not providing treatment.

Of those veterinarians with at least 1 horse with PPID under their care, 67.2% (242/360) provided medical treatment, while some chose not to treat (46/360). Eight veterinarians reported using other options such as dietary management, 4 used herbal therapy, 3 used exercise, 3 used acupuncture, 2 used immunomodulation, and I used parasite management. Sixty-six respondents did not describe their treatment recommendations and some reported using different management strategies in different cases (hence the numerator is greater than the denominator), but did not explain what influenced their choices in each case. The most commonly reported form of medical treatment was pergolide mesylate ($n = 271$), with 136 veterinarians using the compounded form and 135 using the commercially available form. Another 6 veterinarians reported using cyproheptadine, 5 used trilostane, and 2 used bromocriptine. As some veterinarians reported using more than 1 product, the sum of treatments exceeded the number of respondents. Most respondents (71.0%, 303/426) indicated that PPID was an important equine disease. Fifty-four percent of veterinarians (228/426) indicated that a new approach to managing or curing the disease was necessary.

Table IV. Distribution of respondents by practice types.

Practice type	Number of respondents	Overall percentage	Percentage of reported practice types
Private practice	274	64.3	92.6
Academia	17	4.0	5.7
Government	3	0.7	1.0
Industry	2	0.5	0.7
Reported	296	69.5	100.0
Unreported	130	30.5	
Total	426	100.0	

The dataset was then limited to veterinarians working in private and academic practice in North America and Europe ($n = 254$). None of the variables examined, including geographic region ($P = 0.61$) or practice type ($P = 0.61$), was associated with the reported prevalence of disease. Similarly, the number of animals reported as being under the care of each respondent did not vary by geographic region ($P = 0.96$). The number of animals under care did vary by practice category ($P = 0.004$), with respondents in equine-only (specialty) practice caring for more horses with PPID than veterinarians in

mixed, small-animal/equine practices and general practice ($P = 0.002$ and 0.001). There was no difference between those in large animal/equine ($P = 0.15$) or large animal practice ($P = 0.64$) and there were no significant differences among other categories.

Equine veterinarians from North America and Europe who were caring for horses with PPID ($n = 208$) typically used a single diagnostic test to determine whether a horse had PPID (median 1, 25% and 75%, IQ 1 to 2; mean: 1.4 +/– 0.63, IQ: 1 to 4), and this number varied by geographic location ($P = 0.046$), but not based on the characteristics of the practice surveyed ($P = 0.13$). Some respondents reported using clinical signs as their only diagnostic test (56/208, 27%). In the final model of factors affecting whether a practitioner used only clinical signs or clinical signs and an additional test to diagnose PPID, the only significantly associated variable was geographic location ($P = 0.01$). The odds of European veterinarians using clinical signs alone to diagnose PPID were greater than for North American veterinarians [odds ratio (OR): 5.35, 95% confidence interval (CI): 2.1 to 14.2].

If veterinarians chose to use a diagnostic test in addition to clinical signs, the most common adjunct test was an investigation of the endogenous adrenocorticotropic hormone (ACTH) level. The final model identifying the factors associated with whether a practitioner chose to diagnose PPID using clinical signs and endogenous ACTH compared to clinical signs and any other additional test included only the number of horses under the care of the veterinarian. Veterinarians caring for less than 5 horses with PPID were more likely to use endogenous ACTH than another test in addition to clinical signs than those veterinarians caring for more than 5 horses with PPID (OR = 5.0, 95% CI 1.3 to 18.9, $P = 0.009$).

None of the factors examined, including geographic region ($P = 0.31$), was associated with whether a respondent decided to treat PPID medically rather than leaving the horse untreated. North American and European respondents' choice of drug to treat PPID included commercial pergolide mesylate ($n = 100$), compounded pergolide mesylate ($n = 98$), cyproheptadine ($n = 5$), trilostane ($n = 3$), and bromocriptine ($n = 2$). Some respondents used more than one drug.

Discussion

The objectives of this survey were to investigate whether veterinarians in different geographic regions used similar strategies to diagnose and treat PPID, while accounting for any differences in the prevalence of PPID as reported by these veterinarians. We encouraged a wide variety of respondents to participate by inviting a spectrum of veterinarians, from those who were in general-mixed practice with at least some equine cases to those in specialty practices where 100% of the caseload was equine.

Eighty-four percent of respondents were caring for at least 1 horse with PPID, with half of veterinarians reporting at least 5 horses with PPID. These data show that most veterinarians servicing the horse industry have to deal with this chronic, debilitating problem. Our results suggest that European veterinarians were more likely than their colleagues in North America to use clinical signs alone for diagnosis. The reason for this difference is intriguing and merits further investigation. By waiting until the pathognomonic clinical appearance of advanced PPID, some European horses might be made to wait longer than necessary for treatment. Given the ready availability of a commercial medical treatment with proven efficacy and few negative sequelae other than the cost of treating an incorrectly diagnosed patient; however, additional diagnostics could potentially be perceived as not being cost-efficient. Unfortunately, the response rate for our study was not sufficient to detect differences, if any, among European countries.

Taking all responses into consideration, 30% of respondents in our survey used clinical signs, i.e., hypertrichosis, as the sole criterion in diagnosing PPID. While this may seem inadequate, hypertrichosis has been reported as having a positive predictive value (PPV) of 90% (21). This is a high value, but the calculation of PPV is intimately associated with the prevalence of disease. Since the authors of that paper selected their case population as being suspicious of PPID and then confirmed the diagnosis by using postmortem examination, the prevalence of disease was high (62%). The specificity and sensitivity of the test was reported as 95% and 71%, respectively. In our study population, in which veterinarians reported a prevalence of 1% of PPID in their practice populations, the use of hypertrichosis alone would generate a PPV of only 14%. The negative predictive value (NPV) in this population, however, is $> 99\%$. The evaluation of hypertrichosis in older horses results in an increased PPV because they have a higher pretest probability of disease (7). The probability of a false positive diagnosis in an aged horse with hypertrichosis should be much lower due in part to the limited list of possible alternative diagnoses. Rohrbach et al (12) reported that 34% of 44 horses and ponies with PPID were diagnosed solely on the basis of hirsutism, with another 23% based on a combination of hirsutism and a dexamethasone-suppression test. The authors stated that, when present, hirsutism was considered to be as accurate as laboratory diagnosis for their diagnoses. However, the sensitivity is not 100% and the resulting NPV in high-risk horses will not be $> 99\%$. Three percent of horses with a pituitary pars intermedia adenoma at necropsy did not show any clinical signs associated with PPID, including hypertrichosis (22,23).

Dybdal et al (24) reported that all horses with PPID had a plasma cortisol concentration of more than 27.6 nmol/L (1 μg/dL) 20 h after dexamethasone administration, whereas all control horses had serum cortisol concentrations less than 27.6 nmol/L (a sensitivity and specificity of 100%). Subsequently, the dexamethasone suppression test was reported to have a sensitivity of 65% and a specificity of 76% in a population in which the diagnosis was ultimately determined by postmortem assessment of the pituitary gland (21). Most respondents in the current study used endogenous ACTH concentration as their adjunct diagnostic test of choice (25,26). This has a reported sensitivity of 80% to 84% with a specificity of 78% to 83% [using different cutoff values, 29.7 pg/mL (27) and 35 pg/mL (28)], using hypertrichosis and 3 or more clinical signs of PPID in seasons other than autumn. It is important to note that early papers citing diagnostic cutoff values may be misleading as they were published before the seasonal variation in ACTH concentration was recognized (29). The differences in the specificity and sensitivity of the dexamethasone suppression and endogenous ACTH tests may explain why the use of the dexamethasone suppression test, as well as the reported risks of inducing laminitis, has fallen out of favor.

For the aged horse with hypertrichosis, an additional test with the previously mentioned specificities and sensitivities (the presence of hypertrichosis and endogenous ACTH testing) only decreases the probability of detecting a false positive (1-Specificity) PPID horse from 5% to about 1%, assuming serial interpretation of the test results from clinical diagnosis followed by the ACTH test. Depending on the estimated prevalence of the disease in that age of horse, the PPV is not substantially improved by using the combined approach, which brings into question the benefit of additional testing to rule in disease in animals with clinical signs. It was interesting to find that veterinarians caring for fewer than 5 horses with PPID were more likely to use corroborative laboratory testing than those caring for more than 5 horses. While the reason for this is not known, we speculate that perhaps veterinarians caring for more animals with PPID are confident in using only clinical signs as they have more experience with the disease.

One limitation of the data obtained from this survey, as well as that in the existing peer-reviewed literature, is that both horses that are confirmed with the disease and those that are only suspected of having PPID are discussed together. Historically, horses that did not have hypertrichosis, despite advancing age, were infrequently tested and there is currently no consensus on a definitive diagnostic test for documenting PPID, especially in its earlier stages. As such, the true prevalence of the disease may be much higher than reported (12,21,30). The extent to which old horses and ponies (> 15 y) are being tested has been subjectively increasing in recent years, especially in the UK and Australia, which are not well-represented in the current survey, and there has been an emphasis on detecting and treating PPID before it becomes a concern to the horse's welfare.

A recent experimental study reported a PPID prevalence of 21.2% in horses over 15 y (based on endogenous ACTH concentration), despite the prevalence of hypertrichosis being only 14.2% (17). In this scenario of an aged horse with no apparent hypertrichosis, the addition of endogenous ACTH testing interpreted in parallel with clinical signs, again with the previously discussed specificities and sensitivities, will improve the sensitivity of a diagnosis of PPID from 71% with clinical signs alone to 95% for animals with a concurrent positive ACTH test (EpiTools epidemiological calculators: http://epitools.ausvet.com.au/content.php?page=2Tests). This shows that the use of adjunct testing methodologies earlier in the disease process or as a screening test in horses over 12 to 15 y of age can allow earlier diagnosis and treatment of the disease. This may improve the health of the horse and extend its usefulness to its owner. Veterinarians can and should strive to diagnose this condition earlier and improve the quality of life for aging horses.

Most respondents reported treating individuals suspected of having PPID with pergolide mesylate. Commercial and compounded product was equally represented overall. Unfortunately, the survey did not explore the availability to the respondents of the commercial as opposed to the compounded form of pergolide, as this may have significantly affected their choice of product. This is especially true as it has been shown that compounded pergolide has substantial limitations (31,32).

Almost 80% of the small number of participants who explained why they did not treat affected horses reported that financial limitations as well as perceived and practical management limitations reported by their clients precluded treatment. Some veterinarians cited both reasons. This may explain why more than 50% of respondents stated that they would like to see a new treatment or cure developed for this debilitating condition, despite the availability of a drug with proven efficacy (30,33–36). The current treatment is costly because it is ongoing, which makes it labor- and management-intensive. While treating a horse on a daily basis may not seem overly onerous, in extensively managed or pasture-managed horses that are infrequently handled during the off-season, the need to administer daily medication could preclude treatment. In addition, caregivers of both animals and humans with chronic ongoing diseases are subjected to significant emotional stress (37,38). Earlier diagnosis of this condition could improve the welfare of the horse by reducing or preventing some of the clinical sequelae, but will do little to assuage the client concerns and emotional stress about the feasibility of daily medication. If an equally efficacious yet much less labor-intensive treatment were to become available, more veterinarians and clients would be likely to explore this option.

The data from this survey represent the information shared by veterinarians who were interested enough in this issue to take the time to respond to the survey. Volunteer bias is a limitation of information obtained by survey, as it is for the recruitment of practices to provide access to client data. The results were not restricted to veterinarians with a strong interest in PPID, however, as only 71% of respondents identified it as an important disease.

Using third parties to distribute the survey link presented another challenge. As the total number of member e-mails for each distributing organization was not shared and we knew only the total number that responded, we were unable to calculate a response rate. Considering the increasing focus on the privacy and confidentiality of distribution lists, we were fortunate that these organizations were willing to distribute the survey link. The number of respondents was lower than we had originally hoped, although we did have adequate power to explore regional differences and risk factors for important diagnostic and treatment practices based on the resulting confidence intervals. Most respondents were from North America, Europe and, to a lesser extent, the Asia-Pacific region. As far as the authors know, however, this is the only study to provide a concurrent comparison among these regions. While it may be limited in its accuracy, our data reflect a larger cross-section of clinics and geographic regions than has been previously reported. This suggests that there was no substantial difference in the perceived prevalence of PPID among participating regions. It is not known why there were less responses from regions other than Europe and North America.

Finally, while recall biases are inherent in all survey responses, there is no reason to believe that this would differ among regions. The risk of reporting errors was greater for the estimated prevalence of the disease than for routine diagnostic and management practices. As it was not considered practical to ask veterinarians to do a search of their client records, the focus of our discussion has been on diagnostic and treatment choices.

In conclusion, the results of this international survey of equine veterinarians indicated differences in how veterinarians diagnose PPID, with European veterinarians more likely to make a diagnosis without adjunct laboratory testing than their North American colleagues. The estimated prevalence of the condition recognized by

practitioners was approximately 1%, with no apparent geographic variation. More specifically, there was no difference in reported prevalence between the northern and southern hemispheres and no difference between Canada and the US. There is a need for additional treatment options for PPID as veterinarians reported that their clients are concerned about cost and management restrictions related to the long-term treatment of PPID.

Supplemental Material A

1. Do you currently have a horse (or horses) in your practice with PPID (equine Cushing's disease)? If your answer is "No," please skip to question 11.
   ○ Yes
   ○ No

2. Approximately how many horses do you have with this problem and what percentage of your equine patients have this condition? (2 answers please).
   _____
   _____

3. What is the approximate mean (average) age of these horses?
   _____

4. How was the diagnosis made (in most cases)? Check as many as necessary.
   ☐ Clinical signs alone
   ☐ Clinical signs and endogenous ACTH concentration
   ☐ Clinical signs and a dexamethasone suppression test
   ☐ Clinical signs and an ACTH stimulation test
   ☐ Clinical signs and combined dexamethasone suppression/TRH stimulation test
   ☐ Other (please specify):_____

5. Are you treating these horses for the primary disease process (pituitary dysfunction or pituitary tumor)? If your answer is "No," then please skip to Question 8.
   ○ Yes
   ○ No

6. Collectively, how are you treating these horses?
   ☐ Benign neglect/monitoring
   ☐ Medically
   ☐ Other (please specify):_____

7. What medical treatments are you using (check all that apply)? Please skip to Question 11 after completing this question.
   ☐ Commercial pergolide mesylate
   ☐ Compounded pergolide
   ☐ Commercial bromocriptine mesylate
   ☐ Commercial trilostane
   ☐ Commercial cyproheptadine
   ☐ Other (please specify):_____

8. If you are not treating these horses, why not?
   ☐ Client limitations
   ☐ Drugs not available
   ☐ Treatment not warranted
   ☐ Other (please specify):_____

9. If client limitations prevent treatment, why?
   ☐ Financial limitations
   ☐ Management limitations (cannot treat as recommended)
   ☐ Other (please specify):_____

10. If treatment is not warranted, why?
    ☐ Age of horse
    ☐ Disease not deemed to be of concern (by client or veterinarian)
    ☐ Other (please specify):_____

11. Do you perceive this disease to be an important equine health issue?
    ○ Yes
    ○ No
    Please provide additional comments below if necessary:
    _____
    _____
    _____
    _____

12. Do you think that we need a new way to treat (or cure) this disease?
    ○ Yes
    ○ No
    Please provide additional comments below if necessary:
    _____
    _____
    _____
    _____

13. Which of the following best describes your practice situation?
    ○ Private practice
    ○ Academia
    ○ Government institution
    ○ Military
    ○ Other (please specify):_____

14. Which of the following best describes your practice focus?
    ○ Equine only/speciality
    ○ Large animal (equine predominant)
    ○ Large animal (general)
    ○ Small animal/equine
    ○ General mixed practice
    ○ Other (please specify):_____

15. Please provide your COUNTRY of practice (analysis of prevalence by country will be performed)_____

Supplemental Material B

List of General and Equine Veterinary Medical Groups that passed the survey link to their e-mail lists, posted a link on their web pages or sent the link in newsletters.

CVMA—Canadian Veterinary Medical Association
OVMA—Ontario Veterinary Medical Association
SVMA—Saskatchewan Veterinary Medical Association
ABVMA—Alberta Veterinary Medical Association
Ordre des médecins vétérinaires du Québec
NSVMA—Nova Scotia Veterinary Medical Association
AAEP—American Association of Equine Practitioners
American Board of Veterinary Practitioners
American College of Veterinary Internal Medicine—List Server
European College of Veterinary Internal Medicine—List Server
Oklahoma Veterinary Medical Association
BEVA—British Equine Veterinary Association
GPM—German Equine Veterinary Association
AVEF—Association Veterinaire Equine Francaise
AVME (Portugal)—Associação de Médicos Veterinários de Equinos
AVEEC—Associacio de Veterinaris Especialistes en Equids de Catalunya
SIVE—Società Italiana Veterinari per Equini
Norwegian Association of Horse Practitioners
Swedish Equine Veterinary Association
NZEVA—New Zealand Equine Veterinary Association
AEVA—Australian Equine Veterinarian Association
Veterinary Surgeons' Board of Tasmania
Veterinary Surgeons' Board of Western Australia
SAEVA—South African Equine Veterinarian Association
Chilean Association of Equine Veterinarians
RCVS Charitable Trust
VetsOnline
VIN.com
vetsurgeons.org
thehorse.com
Mark Andrews Equine Science Updates

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