*J Vet Intern Med* 2011;25:1144–1151

# Computed Tomographic Findings in the Pituitary Gland and Brain of Horses with Pituitary Pars Intermedia Dysfunction

A.P. Pease, H.C. Schott II, E.B. Howey, and J.S. Patterson

**Background:** Pituitary pars intermedia dysfunction (PPID) is the most common endocrinologic disorder of aged horses.

**Hypothesis/Objectives:** Pituitary glands of PPID-affected horses are larger than those of aged horses without signs of PPID, and the size difference can be detected using computed tomography (CT) imaging.

**Animals:** Eight horses with clinical signs of PPID and supportive endocrinologic test results and 3 aged control (PPID-negative) horses.

**Methods:** Computed tomography examination of the brain and pituitary gland was performed twice in 10 of the 11 horses, approximately 6 months apart. Six PPID-affected horses were treated with pergolide for 6 months between CT scans. The second CT scan was followed by euthanasia and pathologic examination of 6 PPID-affected horses (4 treated horses).

**Results:** On initial examination, pituitary glands of PPID-affected horses were larger in height ($P < .01$) and width ($P < .01$) than controls, but the difference in length was not significant ($P = .06$). After 6 months of pergolide treatment of PPID-affected horses, pituitary gland length increased ($P < .05$), but height and width were not different from pretreatment values. There was no difference between pituitary gland measurements made at the terminal CT scans and necropsy. Furthermore, pituitary gland volume calculated from the measurements was highly correlated to pituitary gland weight. Additional CT findings were bilaterally symmetrical mineralization in the thalamus and cholesterol granulomas adjacent to the lateral and fourth ventricles.

**Conclusions and Clinical Importance:** CT is a useful imaging modality to determine pituitary gland size of PPID-affected horses,and CT measurements are similar to gross pathologic measurements.

**Key words:** Computed tomography; Cushing's; Equine; Pergolide.

Pituitary pars intermedia dysfunction (PPID) in horses, also known as equine Cushing's disease, is the most common endocrinologic disorder of older horses.[1–3] Although there is no evidence that the prevalence of PPID is increasing, diagnosis and treatment of PPID in clinical practice has increased over the past decade. In Queensland, Australia, clinical problems consistent with PPID occurred in 15% of nearly 1000 horses and ponies 15 years of age and older. Increased plasma concentrations of adrenocorticotropin (ACTH) and α-melanocyte stimulating hormone (α-MSH), supportive of PPID also were found in approximately 14% of a subgroup of 300 of these equids.[a]

**Abbreviations:**

| | |
|---|---|
| α-MSH | α-melanocyte stimulating hormone |
| ACTH | adrenocorticotropin |
| CT | computed tomography |
| DST | dexamethasone suppression test |
| PACS | picture archiving and communication system |
| PDH | pituitary dependent hyperadrenocorticism |
| PI | pars intermedia |
| POMC | pro-opiomelanocortin |
| PPID | pituitary pars intermedia dysfunction |
| ROI | region of interest |
| SD | standard deviation |

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*Submitted April 10, 2011; Revised May 26, 2011; Accepted July 7, 2011.*



*10.1111/j.1939-1676.2011.00784.x*

The classic sign of PPID is hypertrichosis, a long and shaggy hair coat that fails to shed, but the primary clinical problem is chronic laminitis in nearly 50% of PPID-affected equids.[3] In humans and dogs, Cushing's disease is most commonly attributed to a corticotroph adenoma in the pars distalis of the pituitary gland. These adenomas are thought to arise spontaneously.[3] In contrast, PPID in horses is attributed to melanotrope hyperplasia and micro- and macroadenoma formation in the pituitary pars intermedia (PI) with resultant overproduction of pro-opiomelanocortin (POMC).[3,4] Recent studies support a pathophysiology of PPID that may parallel that of Parkinson's disease: progressive degeneration of hypothalamic dopaminergic neurons associated with accumulation of aggregates of a misfolded protein, α-synuclein, in nerve terminals.[5] This neuronal damage may be a consequence of oxidant-induced injury.[6] In normal horses, hypothalamic dopaminergic neurons provide tonic inhibition to PI melanotropes, thereby limiting production of POMC.

Pergolide has been described as an effective treatment for PPID for several decades.[2,3,7] As a dopamine-type 2 receptor agonist, the drug is thought to increase dopamine production and suppress POMC production and release, thereby controlling clinical signs of PPID. Pergolide initially was developed and approved for use in the treatment of Parkinson's disease in 1988, but was withdrawn from the human market in 2007 because of adverse effects of valvular fibrosis and regurgitation.[8] Limited data on the pharmacokinetics of pergolide after oral administration to horses (single dose of 0.01 mg/kg) suggest that the drug actually may be more bio-available in horses than people.[9] However, whether pergolide treatment reverses PI hyperplasia and adenoma formation or not has not been investigated.

Various imaging modalities have been used to document enlargement of the pituitary gland in equids with PPID. Contrast-enhanced radiography, using a catheter advanced retrograde via the facial vein to the pituitary fossa, was an early method used to outline enlarged pituitary glands in PPID-affected equids.[10] As computed tomography (CT) imaging was introduced to equine medicine, this modality was used to image enlarged pituitary glands in several reports of horses with PPID[11–13] and was subsequently described as a useful imaging modality to allow accurate measurement of the size of equine pituitary glands in normal horses.[14] A more recent report also documented enlarged pituitary glands by CT imaging in 7 horses with clinical signs and dexamethasone suppression test (DST) results supportive of PPID.[15] In addition to allowing detection of enlarged pituitary glands, dynamic CT imaging after contrast administration has been used to detect micro- and macroadenomas within the pituitary gland of dogs and humans.[16–19]

In this study, we tested the hypothesis that pituitary glands of PPID-affected horses are larger than those of aged horses without signs of PPID, and that this size difference can be detected by CT imaging. Next, the dynamic pattern of contrast medium uptake was investigated. Furthermore, we also investigated whether or not the pituitary gland would decrease in size in a subset of PPID-affected horses after treatment with pergolide.

## Materials and Methods

Eight horses (mean, 24 ± 4 years; range, 18–28) with PPID were diagnosed on the basis of hypertrichosis and supportive DST results, and 3 aged horses (mean, 24 ± 5 years; range, 20-29) without hypertrichosis and with normal DST results were studied. The horses were all from Michigan and had been donated for study, and all procedures performed were approved by the Institutional Animal Care and Use Committee. On the day of CT imaging, two 14-gauge, 5.25-inch catheters were placed into each jugular vein before induction of general anesthesia. Once anesthetized, horses were hoisted onto a custom-designed table that was connected to the CT scanner.[b] Horses were positioned in dorsal recumbency with the head and neck extended and the head was secured as straight as possible. The head was initially imaged using contiguous 2.5-mm slices and images were processed with a standard algorithm. A dose of 250 mL of diatrizoate meglumine-diatrizoate sodium[c] subsequently was administered IV through one of the jugular catheters. During the injection, dynamic imaging was performed by acquiring an image every 2–9 seconds over the central region of the pituitary gland for a period of 3 minutes to assess uptake characteristics and dilution rates of the contrast medium as well as to examine pituitary gland perfusion. After these images had been acquired, a helical CT scan through the entire brain was performed approximately 3 minutes after contrast administration using the same parameters as the precontrast scan. Total imaging time was less than 10 minutes. All horses initially were imaged in January and February 2009, and 10 of 11 horses recovered from anesthesia without incident (euthanasia was performed on 1 control horse before recovery).

Six PPID-affected horses (weight, 435 ± 23 kg) subsequently were treated with pergolide[d] (1 mg/d, PO) orally for 6 months. During that time, all horses were housed at pasture with supplemental hay feeding until pasture grass was available. Clinical improvement (less lethargy, greater hair coat shedding, and weight gain [weight after treatment, 462 ± 45 kg]) was apparent in all 6 treated horses after 3 months and DST results were normal in 3 of 6 horses. For the 3 horses with abnormal DST results, the dose of pergolide was increased to 2 mg/day, whereas the other 3 horses were maintained at 1 mg/day. After 6 months of treatment, improved shedding of hair coat was observed in all treated horses, although 1 horse with a history of chronic laminitis had an exacerbation of laminitis when spring pasture became available. DST results were normal in 3 of 6 horses at this time (1 horse on 1 mg/day and 2 horses that had been increased to 2 mg/day still had abnormal results). One of the nontreated PPID horses remained fairly healthy (with persistent hypertrichosis) during the 6-month period after the initial CT scan, whereas the other horse had exacerbations of chronic laminitis and developed fungal keratitis prompting unilateral enucleation. DST results in these 2 horses remained abnormal. The 2 aged control horses also remained healthy during this period, and DST results 6 months after the initial CT scan remained normal.

Between 6 and 7 months after the initial CT scan (August and September 2009), the 10 horses were again placed under general anesthesia and reimaged. Both survey and contrast-medium[c] (250 ml, IV) enhanced images were obtained, but dynamic studies were not performed. After CT imaging was completed, euthanasia of 6 PPID horses (4 treated and 2 untreated) was performed by administration of sodium pentobarbital (100 mg/kg, IV) and the other 4 horses recovered uneventfully. Within 30 minutes of euthanasia, brains and pituitary glands were removed, pituitary glands were weighed (nearest 0.1 g), and height, width, and length were measured to the nearest millimeter with a ruler. The tissues were sectioned along a midline sagittal plane and placed in formalin. After fixation, tissue blocks were prepared and slides were stained with hematoxylin and eosin for histopathologic examination.

Analysis of contrast medium enhancement and duration of enhancement during the initial dynamic CT scan was performed at the CT workstation using an elliptical region of interest (ROI) analysis, plotting attenuation in Hounsfield units over time. The images were sent to the picture archiving and communication system (PACS) server[e] and then exported to eFilm.[f] All images were interpreted by a board-certified radiologist (APP) who was blinded to the horse's PPID or treatment status. Overall enhancement of the pituitary gland was assessed by Hounsfield unit enhancement. Pituitary gland measurements were made using post-contrast-enhanced images with reconstruction in dorsal and sagittal planes to aid in measurement. Height (dorsoventral), width (left-right), and length (rostrocaudal) were measured on all horses at both time points.

Statistical analysis was performed with a statistical software package.[g] Data are expressed as mean ± standard deviation (SD), and significance was set at $P < .05$. Paired *t*-tests were used to compare pituitary gland measurements between the 2 CT studies for each horse and between the final CT measurements and necropsy measurements. CT measurements of PPID-affected and control horses were compared with an unpaired *t* test. Pearson product moment correlation analysis was performed between CT and necropsy measurements and pituitary gland weights and Bland-Altman plots were constructed to assess bias and level of agreement (±1.96 SD) between CT and necropsy measurements. Next, pituitary gland volume was estimated using the formula for the volume of an ellipse:

$$\text{Volume} = 4/3 \times \pi \times abc$$

where *a*, *b*, and *c* are the radii of height, width, and length, respectively. Estimated volume then was compared with pituitary gland weight by correlation analysis, and bias and level of agreement for the CT and necropsy measurements were assessed. Finally, percent accuracy of CT measurements, assuming necropsy measurements as 100% accurate, was calculated as previously described:[15]

$$\text{Accuracy} = 100 \times (1 - [\text{necropsy measurement} - \text{CT measurement}]/\text{necropsy measurement}).$$

## Results

The pituitary gland could be well imaged in all CT studies, especially after contrast administration (Fig 1). As the pituitary gland is surrounded by a small amount of fat and cerebrospinal fluid in the subarachnoid space, addition of contrast medium provided greater contrast between the vascular pituitary gland and the surrounding structures. During the dynamic studies, time to peak contrast enhancement ranged from 30 to 72 seconds after the start of injection with a mean of 45 ± 12 seconds. Contrast enhancement persisted above baseline for more than 3 minutes after the contrast medium was administered. All pituitary glands had uniform contrast enhancement patterns and no difference in enhancement was observed between PPID-affected and control horses.

Measurements of pituitary gland height, width, and length determined by CT for PPID-affected and control horses are presented in Table 1. Pituitary glands of PPID-affected horses were greater in height ($P < .002$) and width ($P < .01$) but the difference in length ($P = .06$, power =0.05) was not significant when compared with the small group (n = 3) of control horses. When pituitary gland measurements were compared in 6 PPID-affected horses before and after treatment with pergolide for 6 months, no decrease in pituitary gland size was observed. In fact, pituitary gland length was actually greater ($P < .03$) after treatment.

Measurements of pituitary gland height, width, and length determined at necropsy for 6 PPID-affected horses (4 treated and 2 untreated) were 18.7 ± 7.3, 24.2 ± 2.3, and 27.0 ± 1.3 mm, respectively. CT measurements of height, width, and length for these same 6 horses were 17.8 ± 3.8, 25.0 ± 2.0, and 24.8 ± 1.9 mm, respectively. Bland–Altman plots constructed to assess bias and levels of agreement for pituitary gland measurements, determined at the final CT examination and at necropsy, showed no systematic trends although the greatest difference was found for length (necropsy minus CT measurements: height bias 0.8 ± 10.5 mm, width bias 0.8 ± 7.1 mm, and length bias 2.1 ± 4.2 mm). Furthermore, for all CT and necropsy examinations, measurement ranges were greater for height (CT, 5–22 mm; necropsy, 10–30 mm) than for width (CT, 16–28 mm; necropsy, 20–27 mm) or length (CT, 16–28 mm; necropsy, 25–28 mm).

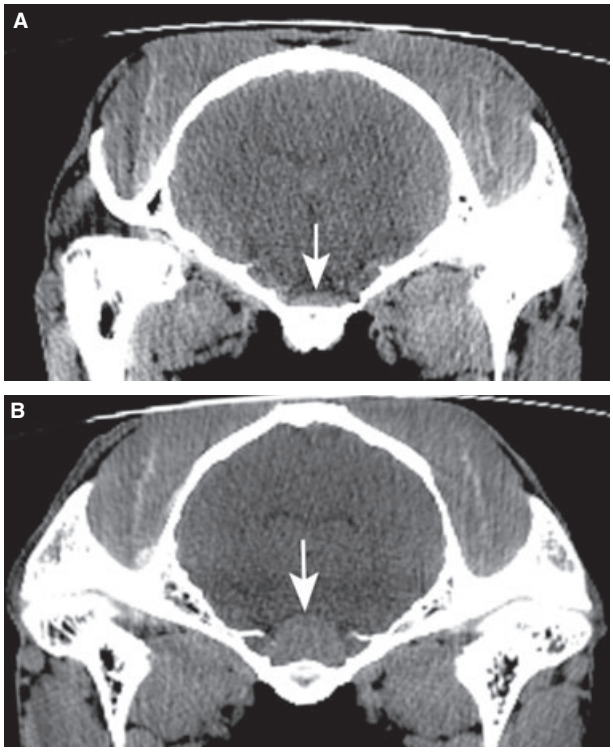


**Fig 1.** Contrast-enhanced transverse computed tomographic images of the skull at the level of the sella turcica of an aged control horse (**A**) and a horse with PPID (**B**); note the enlarged pituitary gland of the PPID-affected horse at the base of the brain.

Pituitary gland weight ranged from 4.3 to 10.1 g and a histopathologic grade of 5 (adenoma >5 mm diameter)[4] was found in all 6 PPID-affected horses. Pearson product moment correlations between CT or necropsy measurements and weight were not significant except for CT length measurements and necropsy height measurements (Table 2). When measurements were used to estimate pituitary gland volume and these values were compared with pituitary gland weight, significant correlations were found between both CT and necropsy measurements and weight (Fig 2). Bias and level of agreement for calculated pituitary gland volume showed that CT measurements slightly underestimated pituitary gland volume, when compared with necropsy measurements (necropsy minus CT measurements: 0.26 ± 1.39 $cm^3$), although measurements from 1 horse (bias 1.9 $cm^3$) may have skewed overall bias

**Table 1.** Mean ± SD measurements of pituitary gland height, width, and length in 8 pituitary pars intermedia dysfunction (PPID)-affected horses and 3 aged control (non-PPID-affected) horses determined by computed tomographic (CT) imaging; pre values were measured from CT examinations performed in January and February 2009 and post values were measured from CT examinations performed in August and September 2009.

| Group | Height (mm) | Width (mm) | Length (mm) |
|---|---|---|---|
| PPID, pre (n = 8) | 15.8 ± 2.3[a] | 23.3 ± 2.4[a] | 22.1 ± 2.4[a] |
| Non-PPID, pre (n = 3) | 8.7 ± 3.2[b] | 17.7 ± 2.9[b] | 18.3 ± 3.2[a] |
| PPID, treated, pre (n = 6) | 15.2 ± 2.3[a] | 22.3 ± 2.1[a] | 21.5 ± 2.1[a] |
| PPID, treated, post (n = 6) | 15.5 ± 3.7[a] | 23.8 ± 1.2[a] | 23.7 ± 1.4[b] |
| PPID, untreated, pre (n = 2) | 17.5 ± 0.7 | 26 ± 0.0 | 24 ± 2.8 |
| PPID, untreated, post (n = 2) | 20.5 ± 0.7 | 27 ± 1.4 | 26.5 ± 2.1 |
| Non-PPID, pre (n = 2) | 10.5 ± 0.7 | 18.5 ± 3.5 | 19.5 ± 3.5 |
| Non-PPID, post (n = 2) | 12.0 ± 1.4 | 22 ± 4.3 | 21 ± 2.8 |

[a]Different superscripts within a column, between lines, indicate a significant difference, $P < .05$; comparisons were not made between groups with only 2 animals.

(Fig 3). Overall, accuracy of CT measurements, in comparison to necropsy measurements, was good with values of 104 ± 32% (range, 70–160%), 105 ± 16% (range, 85–130%), 92 ± 8% (range, 81–100%), and 97 ± 19% (range, 65–120%), respectively, for pituitary gland height, width, length, and volume.

An additional finding in all horses with PPID and in 2 of 3 control horses was symmetrical mineralization in the thalamus. Further, presumed cholesterol granuloma formation was apparent in the lateral ventricles (2 horses) and in the 4th ventricle (2 horses) with 1 horse having both mineralization of the thalamus and a presumed cholesterol granuloma in the 4th ventricle (Fig 4). Histopathologic examination of the thalamus, targeted to the areas of mineralization observed on CT, was performed just caudal to the optic chiasm (5 mm caudal to the cranial border of the thalamus) and immediately caudal to the pituitary stalk (to identify the hypothalamic nuclei). Intensely basophilic, globular foci of mineralization (up to 1 mm diameter) were confirmed in both sections of 4 of the 6 horses. Some foci were associated with blood vessel walls, whereas others were not (Fig 5).

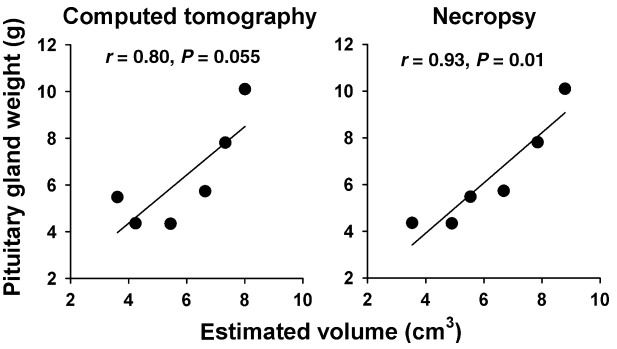


**Fig 2.** Pearson product moment correlations between pituitary gland weight and volume determined by computed tomography (left panel) and at necropsy (right panel).

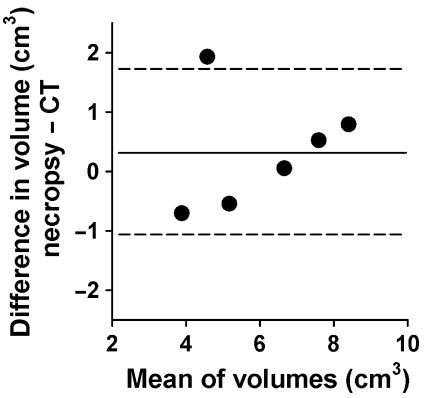


**Fig 3.** Bland–Altman plot showing bias (solid line) and levels of agreement (±1.96 SD, dashed lines) in estimated pituitary gland volume calculated from measurements determined by computed tomography and at necropsy.

## Discussion

Although CT imaging of an enlarged pituitary gland in a horse with PPID initially was reported more than 20 years ago,[11] to date, no substantive evaluation of static or dynamic contrast enhancement of the pituitary gland or comparison of CT and necropsy measurements in PPID-affected horses has been performed. In this study, CT imaging correctly identified an enlarged pituitary gland in all PPID-affected horses, when compared with aged control horses. Furthermore, the pituitary gland was better outlined after contrast administration in all horses. Case selection, with all PPID-affected horses submitted for necropsy examination having PI macroadenomas, probably contributed to the diagnostic success of CT. In horses with

**Table 2.** Pearson product moment correlation coefficients and significance for pituitary gland weight and measurements determined by computed tomographic (CT) and at necropsy in 6 horses with pituitary pars intermedia dysfunction (PPID); significant correlation in bold font.

| Group | Height | Width | Length |
|---|---|---|---|
| CT measurements | $r = 0.58$, $P = .23$ | $r = 0.55$, $P = .25$ | **$r = 0.82$, $P < .05$** |
| Necropsy measurements | **$r = 0.96$, $P < .01$** | $r = 0.63$, $P = .13$ | $r = 0.09$, $P = .86$ |

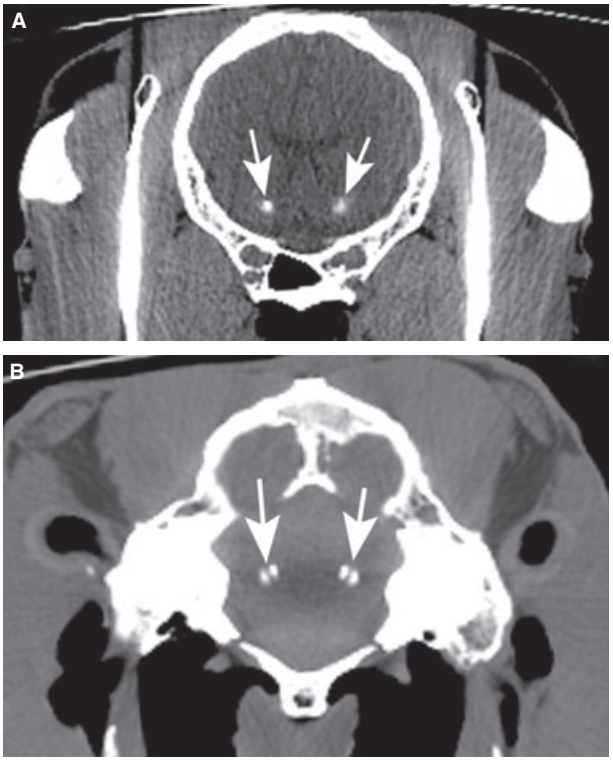


**Fig 4.** Transverse computed tomographic images of the skull of two PPID-affected horses. Image **A** shows the bilaterally symmetrical areas of mineralization within the thalamus and image **B** shows the cholesterol granulomas within the lateral apertures of the 4th ventricle.

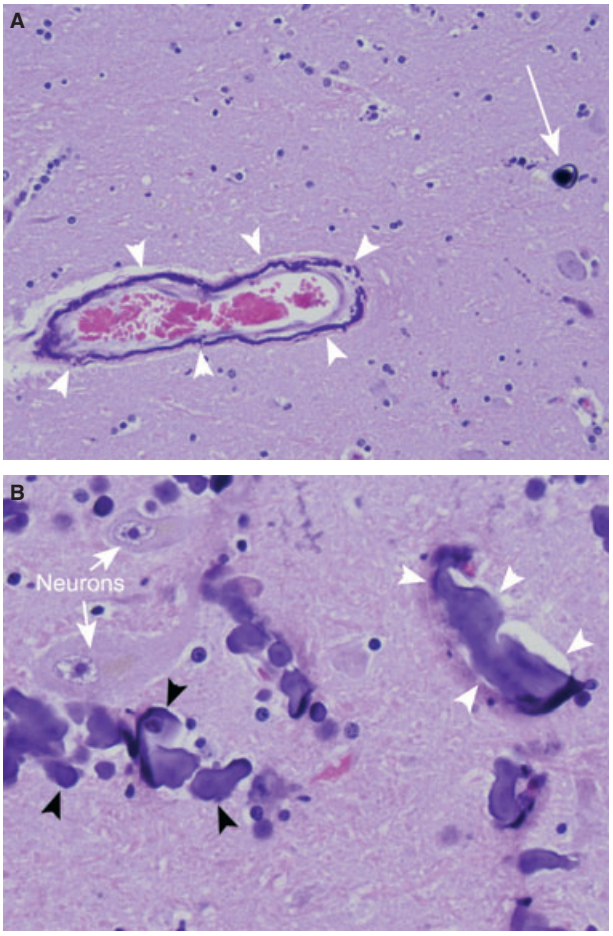


**Fig 5.** Histopathological sections of the thalamus of a PPID-affected horse, cut transversely and immediately caudal to the pituitary stalk. **A** = 200x; areas of mineralization were intensely basophilic and could be found circumferentially in blood vessel walls (arrowheads) or as globular foci of mineralization (up to 1 mm diameter; arrow). **B** = 400x; some areas of mineralization were associated with blood vessel walls (white arrowheads), whereas others were not associated with blood vessel walls (black arrowheads).

less severe grades of PPID (PI hyperplasia or microadenoma formation)[4] and minimal increase in overall pituitary gland size, CT imaging would be unlikely to detect these changes.[14,17,19]

In this study, dynamic contrast enhancement revealed uniform uptake and elimination patterns in all pituitary glands, with no apparent differences between PPID-affected and control horses. Uniform contrast enhancement was an unexpected finding because dogs with pituitary dependent hyperadrenocorticism (PDH) often have displacement of the distinct contrast enhancement of the neurohypophysis (pituitary flush) or less contrast enhancement than normal pituitary glands.[18] The lack of a difference in contrast enhancement between normal and abnormal pituitary glands in this study could be a consequence of the low number of control horses as well as the fact that control horses were also aged. It would be of interest to compare dynamic CT findings in a group of young horses with those of a group of PPID-affected horses.

In normal horses, the pituitary gland typically weighs between 2 and 4 g, with the largest glands found in pregnant and lactating mares, in association with mild enlargement of the pars distalis.[14,20] A necropsy study of 100 pituitary glands collected from horses without clinical signs of PPID reported age-related increases in both pituitary gland weight and height, as well as in presence of histologic lesions in both the PI and pars distalis.[20] Mean pituitary gland height, width, and length ranged from 10 to 12 mm, 19 to 21 mm, and 21 to 24 mm, respectively, in these normal horses. In contrast, in 19 horses with PPID, pituitary gland weight was 7.7 ± 3.3 g (maximum, 13.9 g) and pituitary gland height, width, and length were 19.2 ± 4.3 mm, 24.2 ± 2.6 mm, and 26 ± 3.1 mm, respectively (maximum, 27 × 29 × 33 mm). These values were all significantly greater than those found in horses without clinical signs of PPID.[20] Similar to the findings in these horses, the largest difference in pituitary gland size between PPID-affected and normal horses was in pituitary gland height. The likely explanation for a greater increase in height of the pituitary gland, when compared with width or length with macroadenoma formation, is the confined location of the pituitary gland within the hypophyseal fossa of the sphenoid bone. Although the pituitary gland is

surrounded by fibrovascular tissue within the hypophyseal fossa, the incomplete diaphragma sellae, between the dorsal surface of the gland and the overlying hypothalamus, provides the path of least resistance for gland expansion.

In a previous report that described post-mortem, static CT imaging of normal equine pituitary glands, accuracy of contrast-enhanced CT measurements (collected in both contiguous or overlapping slices of 4 and 10 mm), when compared with necropsy measurements, was reported to be good for pituitary gland width and length, but CT underestimated height by 30–40%. Furthermore, accuracy of pituitary gland volume determined by CT reconstruction and tracing, underestimated necropsy measurements by 40–50%.[14] The authors of this report speculated that the low dose of contrast agent administered (60 mL) may have resulted in incomplete pituitary gland enhancement and that beam hardening artifacts from the temporomandibular joints may have obscured visualization of the dorsal margin of the pituitary gland. In our study of live horses using nearly 3 times the amount of contrast agent, CT measurements were more accurate when compared with necropsy measurements and beam hardening artifacts were not a problem, probably because of increased sensitivity of the multislice CT scanner, when compared with single slice CT scanners. The largest discrepancy was in length (bias and level of agreement of necropsy minus CT measurement of $2.1 \pm 4.2$ mm). As contrast enhancement of both the fibrovascular bundle surrounding the pituitary gland and the gland itself appear similar on CT imaging,[14] CT measurement could be expected to overestimate actual pituitary gland size; however, the opposite was observed. However, closer scrutiny of the data revealed that discrepancies in length measurements were large in both directions (range 6–9 mm). Thus, underestimation of pituitary gland length is not considered to be a true artifact of CT measurement, especially in the small group of horses studied. Next, if CT measurements are accurate, significant correlations could also be expected between CT measurements and pituitary gland weight (Table 2); however, the only significant association was between length and weight (although correlation coefficients were >0.5 for both height and width, suggesting that correlations may have been significant if a larger number of horses were studied). Curiously, the only significant correlation between necropsy measurements and pituitary gland weight was for height (Table 2) that was not unexpected because this measurement had the widest range of values. The other nonsignificant correlations can probably be attributed to the narrow measurement ranges, especially for width and length, as well as the small number of horses ($n = 6$). Some of the discrepancy between CT and necropsy measurements also could result from a change in the dimensions of the gland after removal from the hypophyseal fossa.[14] Not surprisingly, when measurements were combined to calculate pituitary gland volume, correlations with weight became highly significant for both CT and necropsy measurements (Fig 2). Furthermore, for assessment of agreement between 2 methods of measurement, Bland–Altman analysis is more appropriate than correlation analysis[21] and this analysis, although limited to 6 data points, revealed minimal bias between CT and necropsy calculations of pituitary gland volume (Fig 3).

To our knowledge, this is the 1st study to investigate whether treatment with pergolide can reverse pituitary gland enlargement in PPID-affected horses. All 6 horses showed improvement in 1 or more clinical signs over the 6-month treatment period and 5 of 6 had normal DST results after either 3 or 6 months. Nevertheless, there was no evidence of a decrease in gland size from the initial to final CT examinations. In fact, pituitary gland length actually increased during the treatment period (Table 1). All CT measurements also increased in the 2 PPID-affected horses that were not treated. Although the number of untreated PPID-affected horses was too small for statistical comparison, whether treatment with pergolide may either arrest or slow further PI enlargement remains unknown. Furthermore, changes in CT measurements may have been confounded by the change in season, as the second examinations were performed in August and September, a time of year when the hypothalamic-pituitary-adrenal axis (HPAA) is upregulated in preparation for winter (in the northern hemisphere).[22]

Another curious CT finding in all PPID-affected horses and 2 of the control horses was bilaterally symmetrical mineralization within the thalamus. In addition, suspected cholesterol granulomas were identified in 4 PPID-affected horses. Mineralization of the thalamus and globus pallidus, especially associated with the vasculature, is considered an age-related change in horses and people,[23–26] However, 40% of dogs with hyperadrenocorticism have dermal mineralization and 90% have microscopic evidence of pulmonary interstitial mineralization.[27] Although dermal and pulmonary mineralization have not been described in PPID-affected horses, and thalamic mineralization and cholesterol granulomas are seen as a normal geriatric change, horses with PPID could be more likely to develop mineralization within the thalamus or cholesterol granulomas when compared with normal aged horses. As a result of the small sample size, this difference warrants further investigation.

Although our study documents that CT is a useful and rapid imaging tool to evaluate pituitary gland size in live horses as well as to monitor changes in pituitary gland size with disease progression or treatment, CT provided minimal information about the internal architecture of the pituitary gland in PPID-affected horses. With introduction of high resolution magnetic resonance imaging (MRI) systems to equine medicine, this imaging modality may provide better detail of the internal structure of the pituitary gland in PPID-affected horses in the future. Nevertheless, despite the fact that CT has less contrast resolution than MRI, CT is more readily available to equine practitioners, requires shorter imaging time, and development of a standing CT scanner obviates the risk and expense of

general anesthesia. Furthermore, both CT and MRI studies are recommended pre-operatively in humans with pituitary gland neoplasia. MRI provides superior anatomical detail of the normal and abnormal areas of the pituitary gland whereas CT is useful in determining whether the neoplasm has invaded the bony structures surrounding the gland.[17] Of interest, a recent study of 11 dogs with PDH found that low field MRI and dynamic CT imaging were able to provide similar information about gland size and changes in contrast enhancement.[19] Thus, CT remains a useful, rapid, and practical tool for evaluation of the pituitary gland in veterinary patients.

In conclusion, contrast-enhanced CT imaging was useful for identification of PI enlargement in PPID-affected horses. Next, treatment of PPID-affected horses with pergolide for 6 months did not result in a decrease in pituitary gland size, although the change in season probably confounded our ability to detect a change. Whether drug treatment may slow PI enlargement or not remains unknown and would require a longer duration of study to determine. However, CT provided a rapid, minimally invasive method to evaluate the pituitary gland in horses and will probably remain a using imaging tool in the future, especially if surgical treatment of this problem of older horses is pursued.

## Footnotes

[a] McGowan TW, Hodgson DR, McGowan CM. The prevalence of equine Cushing's syndrome in aged horses. J Vet Intern Med. 21:Abstract 113;603.

[b] 16 slice, GE Brightspeed GE Healthcare, Milwaukee, WI

[c] MD-76; Mallinckrodt, Hazelwood, MO

[d] Lilly Celance, 1000 ug tablets, pergolide (as mesylate), Pergolide Mesylate Tablets, 1 mg, Elanco Animal Health, A Division of Eli Lilly and Company, Indianapolis, IN

[e] McKesson, San Francisco, CA

[f] Merge HealthCare, Milwaukee, WI

[g] SigmaStat, Systat Software, Inc, Chicago, IL

## Acknowledgments

The authors thank Sue Wismer, Julie Rapson, Lauren Groppi, and Rex Miller for technical assistance and Caroline Baldo, Phyllis Shance, and Molly Lazar for anesthesia services.

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