Special Report

Diagnosis of hyperadrenocorticism in dogs: a survey of internists and dermatologists

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Objective—To determine testing protocols used by board-certified internists and dermatologists for diagnosis of hyperadrenocorticism (HAC) in dogs.

Design—Survey.

Study Population—Board-certified internists and dermatologists.

Procedure—A questionnaire was mailed to 501 specialists to gather information pertaining to diagnosis of HAC.

Results—206 surveys were returned. Only 26% of respondents indicated they would screen a dog for HAC if the dog had only a few laboratory abnormalities consistent with HAC and no clinical signs consistent with the disease; 31% indicated they would not, and 43% indicated they would sometimes. Overall, 55% of respondents indicated they preferred to use the low-dose dexamethasone suppression test for routine screening of dogs suspected to have HAC. However, many respondents indicated they would use a different screening test than usual in particular circumstances. Sixty-eight percent of respondents indicated they would perform a second screening test for confirmation if results of an initial screening test were positive but there were few clinical or laboratory abnormalities consistent with HAC. Most respondents used some sort of test to differentiate pituitary-dependent HAC from HAC secondary to an adrenal tumor (AT), but no 1 test was clearly preferred. Ultrasonography was commonly used, whereas computed tomography and magnetic resonance imaging were not, even if available.

Conclusions and Clinical Relevance—Results suggest that the low-dose dexamethasone suppression test is the test most commonly used to screen dogs for HAC but that other tests may be used in certain circumstances. A variety of tests were used to differentiate pituitary-dependent HAC from HAC secondary to an AT. (*J Am Vet Med Assoc* 2002;220:1643–1649)

Hyperadrenocorticism (HAC) is 1 of the most common endocrinopathies in dogs. Naturally occurring HAC is a result of sustained, high plasma cortisol concentrations resulting from excess secretion of ACTH by a pituitary tumor (ie, **pituitary-dependent HAC [PDH]**) or an autonomously functioning **adrenal tumor (AT)**.

Several laboratory tests have been described to screen dogs for HAC and to differentiate the underlying cause in affected dogs; however, the best test or best combination of tests is contentious. The ACTH stimulation test and **low-dose dexamethasone suppression test (LDDST)** are the most commonly used screening tests, but each has advantages and disadvantages. The ACTH stimulation test is shorter and requires 1 to 2 hours, depending on the protocol used, but in most studies,[1,2] it was less sensitive than the LDDST. This is especially apparent in dogs with AT, in which sensitivity of the ACTH stimulation test may be as low as 59%.[3] In contrast, the ACTH stimulation test may be the more specific test, especially in dogs with nonadrenal illness.[2,4] The combination test (**high-dose dexamethasone suppression test [HDDST]** followed by ACTH stimulation test) is used to screen dogs for HAC and differentiate the underlying cause in affected dogs during a single testing period. As a screening test, it is no more sensitive or specific than the ACTH stimulation test alone. Moreover, its ability to both screen and differentiate accurately has been challenged, and use of the combination test is not recommended by at least 1 author.[5] The **urine cortisol:creatinine ratio (UCCR)** has been shown to be very sensitive in several studies,[6-11] even up to 100%, but the specificity in dogs with nonadrenal disease is as low as 21%.[2,10,11]

In dogs with positive screening test results, measurement of endogenous ACTH concentration and the HDDST are the most commonly used methods for differentiating PDH from HAC secondary to an AT. However, the HDDST does not allow such differentiation in approximately 35% of cases[12] and requires collection of 3 blood samples. Measurement of the

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endogenous ACTH concentration requires only a single blood sample, but special handling is required.[13] A differentiation is obtained 71 to 95% of the time.[5,14] Imaging techniques such as ultrasonography, **computed tomography (CT)**, and **magnetic resonance imaging (MRI)** may also be used to differentiate PDH from HAC associated with an AT.

The choice of diagnostic protocol for dogs suspected of having HAC is presumably based on clinical training, experience, and personal preference. The purpose of the study reported here was to survey the specialists most likely to treat dogs with HAC (ie, internists and dermatologists) for information on diagnostic testing protocols they use. We also wanted to determine whether type of specialty, time since completion of residency training, type of practice, number of dogs tested per year, or number of dogs in which HAC was diagnosed per year affected diagnostic choices.

Materials and Methods

Survey and participants—A questionnaire[a] was developed to assess diagnostic protocols used to screen dogs for naturally occurring HAC and differentiate the underlying cause. The survey was mailed to 420 individuals who were diplomates of the **American College of Veterinary Internal Medicine (ACVIM)**, subspecialty of internal medicine; 76 individuals who were diplomates of the **American College of Veterinary Dermatologists (ACVD)**; and 5 individuals who were diplomates of both. To characterize clinical experience, all participants were asked to supply the following information: number of years since completion of residency training; whether they were board certified by the ACVIM, ACVD, or both; whether they were employed in private or university practice; estimated number of dogs tested for HAC per year; and estimated number of dogs in which HAC was diagnosed per year.

To determine diagnostic testing protocols, respondents were asked what general laboratory data they obtained prior to performing a specific screening test for HAC. This included whether dogs that had few or no clinical signs of HAC but had abnormal clinicopathology test results (eg, dogs with polyuria and polydipsia and high serum **alkaline phosphatase [ALP]** activity) were screened for HAC and whether a normal serum ALP activity was sufficient to rule out a diagnosis of HAC. Respondents were also asked about their general preferences for screening tests and screening test methodology and whether a second screening test was used for confirmation. Finally, respondents were asked about their general preferences for differentiation tests and how frequently they performed such tests.

Data analysis—Data were sorted by demographic characteristics of specialty, type of practice, number of dogs tested per year, number of dogs in which HAC was diagnosed per year, and number of years since completion of residency training. The number of years since completion of residency training was categorized as ≤ 5 years, 6 to 10 years, 11 to 15 years, 16 to 20 years, and ≥ 20 years. To evaluate specialty type, responses from internists were compared with responses from dermatologists; individuals board certified by both the ACVIM and ACVD were excluded from these analyses. To evaluate practice type, responses from individuals practicing in a university setting were compared with those from individuals in private practice; respondents who indicated they were in both types of practice or who indicated they were in a different clinical setting (eg, government practice) were excluded from these analyses. Number of dogs tested for HAC and number of dogs in which HAC was diagnosed were categorized as ≤ 5/y, 6 to 10/y, 11 to 20/y, 21 to 30/y, and > 30/y. A Wilcoxon signed rank test was used for comparison of 2 groups, whereas a Kruskal-Wallis test was used for comparison of ≥ 3 groups. A Spearman correlation test was used to assess the relationship between number of dogs tested for HAC and number of dogs in which HAC was diagnosed. For all analyses, values of $P \leq 0.05$ were considered significant.

Results

Respondents—Of 501 surveys mailed, 4 were returned because of incorrect address information, and 8 were returned incomplete. Of the remaining 489 surveys, 206 (42%) were returned completed, and 283 were not returned. Not all respondents answered all demographic questions, and certain respondents were excluded from certain analyses as described. Therefore, the number of responses included in each analysis varied.

Two respondents did not indicate type of specialty. Of the remaining 204, 161 (79%) were internists, and 43 (21%) were dermatologists. Of the 198 respondents who indicated practice type, 83 (42%) were in university practice, and 115 (58%) were in private practice. Of those who responded, the largest number had completed their residency training < 5 years previously (31%; **Table 1**), tested between 11 and 20 dogs for HAC each year (27%), and diagnosed HAC in 6 to 10 dogs each year (37%).

Screening for hyperadrenocorticism—Overall, the number of dogs screened for HAC each year and the number of dogs in which HAC was diagnosed each year were significantly correlated ($r = 0.74$; $P < 0.001$). Only 53 of 205 (26%) respondents indicated that they would screen a dog for HAC if the dog had only a few laboratory abnormalities consistent with HAC (eg, high serum ALP activity) and no clinical signs consistent with the disease, whereas 64 (31%) indicated that they would not, and 88 (43%) indicated that they would sometimes. Willingness to screen dogs without consistent clinical signs for HAC was significantly ($P = 0.03$) associated with the number of dogs in which HAC was diagnosed per year (**Table 2**). For the most

Table 1—Demographics of respondents to a survey of internists and dermatologists regarding protocols for diagnosis of hyperadrenocorticism (HAC) in dogs

Years since completion of residency training		No. of dogs screened for HAC		No. of dogs in which HAC was diagnosed	
No. of years	No. of respondents (%)	No. of dogs/y	No. of respondents (%)	No. of dogs/y	No. of respondents (%)
≤ 5	62 (31)	≤ 5	11 (5)	≤ 5	66 (33)
6–10	56 (28)	6–10	43 (22)	6–10	75 (37)
11–15	44 (22)	11–20	54 (27)	11–20	34 (17)
16–20	27 (13)	21–30	45 (23)	21–30	11 (5)
> 20	13 (6)	> 30	46 (23)	> 30	17 (8)

Table 2—Cross-tabulation of whether respondents to a survey on protocols for diagnosis of HAC in dogs would screen a dog without clinical signs of the disease versus number of dogs in which HAC was diagnosed per year

Screen dogs without clinical signs	No. of dogs in which HAC was diagnosed per year				
	≤ 5	6–10	11–20	21–30	> 30
Yes	10 (15)	19 (25)	16 (49)	5 (46)	3 (18)
No	30 (46)	19 (25)	4 (12)	3 (27)	7 (41)
Sometimes	26 (39)	37 (49)	13 (39)	3 (27)	7 (41)

Data are given as number of respondents (%).

part, the higher the number of dogs in which HAC was diagnosed each year, the more likely that respondents would screen a dog with no clinical signs of disease. Reasons given for deciding whether to screen such dogs included client opinion, clinician level of suspicion, lack of another reason for the high serum ALP activity, persistently high serum ALP activity, and magnitude of the increase in serum ALP activity. Some respondents indicated that testing would be pursued if HAC was believed to be contributing to a coexisting disease, such as recurrent pyoderma or urinary tract infection.

Conversely, if serum ALP activity were within reference limits, 19 of 206 (9%) respondents indicated that they would automatically rule out a diagnosis of HAC, 177 (86%) indicated that they would not, and 10 (5%) were uncertain.

In dogs suspected to have HAC, routine clinicopathologic tests, such as a CBC, a serum biochemical profile, measurement of serum ALP activity, urinalysis, and bacterial culture of a urine sample, may be done to increase or decrease the index of suspicion. Only 3 of 205 (1.5%) respondents indicated that they only perform a serum biochemical profile in such dogs; 1 (0.5%) indicated that he or she only measured serum ALP activity; 14 (7%) indicated that they perform a serum biochemical profile and a CBC; 1 (0.5%) indicated that he or she performed a serum biochemical profile and a urinalysis; 109 (53%) indicated that they perform a serum biochemical profile, CBC, and urinalysis; 45 (22%) indicated that they perform a serum biochemical profile, CBC, urinalysis, and bacterial culture of a urine sample; 1 (0.5%) indicated that he or she performed a serum biochemical profile, urinalysis, and bacterial culture of a urine sample; and 31 (15%) indicated that they performed other combinations of tests.

With regards to the initial test used to screen dogs for HAC, 62 of 205 (30%) respondents indicated that they preferred the ACTH stimulation test, 112 (55%) preferred the LDDST, 11 (5%) preferred the UCCR, and 6 (3%) preferred the combination test. The remaining 14 (7%) indicated that the initial screening test chosen varied, depending on factors such as whether there was a history of exogenous glucocorticoid administration, clinical signs, cost, and client convenience. Reasons cited for preferring these particular tests included client convenience (71 respondents; 35%), high specificity (66; 32%), high sensitivity (98; 48%), a possibility of differentiating the underlying cause while screening for the presence of the disease (75; 37%), and the ability to rule out iatrogenic HAC if the history of glucocorticoid administration was unknown (53; 26%). Other reasons cited included a desire to have results of a baseline ACTH stimulation test before initiation of mitotane treatment, a desire to have 2 positive test results for confirmation of the diagnosis, and the time required for test completion.

Respondents indicated that, on occasion, they would use a test other than the preferred screening test. Reasons for this that were cited include client convenience (89 respondents; 47%), an unclear history of previous glucocorticoid administration (77; 41%), presence of few or no clinical signs (30; 16%), presence of few or no laboratory abnormalities (28; 15%), presence of known nonadrenal illness (59; 31%), and a prior diagnosis of diabetes mellitus (43, 23%). Of the 62 respondents who indicated they would use a test different from their preferred screening test in dogs with nonadrenal illness, 23 (37%) indicated that the ACTH stimulation test was their typical preferred test if nonadrenal illness was not present, 29 (47%) indicated the LDDST was their typical preferred test if nonadrenal illness was not present, 4 (6%) indicated measurement of the UCCR was their typical preferred test if nonadrenal illness was not present, 4 (6%) indicated adrenal ultrasonography was their typical preferred test if nonadrenal illness was not present, and 2 (3%) indicated the combination test was their typical preferred test if nonadrenal illness was not present. Of the 26 respondents who indicated they would choose a different test for screening dogs with few or no clinical signs, 16 (62%) indicated the ACTH stimulation test was their typical preferred test if more clinical signs were present, 8 (31%) indicated the LDDST was their typical preferred test if more clinical signs were present, 1 (4%) indicated measurement of the UCCR was his or her typical preferred test if more clinical signs were present, and 1 (4%) indicated the combination test was his or her typical preferred test if more clinical signs were present. Other reasons given for using a screening test other than the preferred test included current administration of medications such as phenobarbital, a contraindication to injection of a steroid, a lack of availability of ACTH, cost, and a request by the owner that only 1 test be performed.

If results of an initial screening test were positive but there were few clinical or laboratory abnormalities consistent with HAC, 137 of 200 (69%) respondents indicated they would perform a second screening test for confirmation, 56 (28%) indicated they would not, and 7 (4%) indicated they would sometimes. Conversely, if results of an initial screening test were positive and there were many clinical and laboratory abnormalities consistent with HAC, 43 of 205 (21%) respondents indicated they would perform a second screening test for confirmation, and 162 (79%) indicated they would not. If a second screening test was needed for confirmation, 38 of 159 (24%) respondents would use the ACTH stimulation test, 53 (33%) would use the LDDST, 3 (2%) would measure the UCCR, 19 (12%) would perform abdominal ultrasonography, and 46 (29%) would use another test or combination of tests.

If results of an initial screening test were negative and HAC were still suspected, 170 of 205 (83%)

respondents indicated they would perform another screening test to try to establish a diagnosis, 31 (15%) indicated they would not perform a second screening test, and 4 (2%) indicated that they would sometimes. Of the 68 respondents that used the ACTH stimulation test and the 112 that used the LDDST as their preferred initial screening test, 58 (94%) and 87 (78%), respectively, indicated they would perform a second screening test if results of the first were negative. Fifty-one of 171 (30%) respondents indicated that the second screening test they would use in this situation would be an ACTH stimulation test, 65 (38%) indicated they would perform an LDDST, 2 (1%) indicated they would perform a combination test, 3 (2%) indicated they would measure the UCCR, 1 (0.5%) indicated he or she would measure serum activity of the corticosteroid-induced enzyme of ALP, 11 (6%) indicated they would perform abdominal ultrasonography, and 38 (22%) indicated they would perform another test or a combination of tests.

When performing an LDDST, the type of dexamethasone, the route of administration, and the dose can vary. Of 168 respondents who reported type of dexamethasone used, 100 (60%) used dexamethasone sodium phosphate, 54 (32%) used dexamethasone in polyethylene glycol, and 14 (8%) used either. Of the 166 respondents who reported route of administration, 23 (14%) gave dexamethasone IM, 138 (83%) gave it IV, and 5 (3%) gave it IM or IV. Of the 196 respondents who reported dose of dexamethasone, 143 (73%) used a dose of 0.01 mg/kg (0.0045 mg/lb), 49 (25%) used a dose of 0.015 mg/kg (0.0068 mg/lb), and 4 (2%) used either.

In dogs with serious nonadrenal illness such as renal failure, 70 of 202 (35%) respondents indicated that the ACTH stimulation test was their initial screening test of choice, 83 (41%) indicated the LDDST was, 6 (3%) indicated the combination test was, 8 (4%) indicated the UCCR was, 4 (2%) indicated measuring serum activity of the corticosteroid-induced enzyme of ALP was, 8 (4%) indicated abdominal ultrasonography was, 1 (0.5%) indicated abdominal radiography was, and 22 (11%) indicated another test or combination of tests was. For those respondents whose first choice of a screening test, in general, was the ACTH stimulation test or the LDDST, 38 of 62 (61%) and 63 of 112 (56%), respectively, did not change their choice for screening dogs with nonadrenal illness. Four of 202 (2%) respondents indicated they would treat all dogs with serious nonadrenal illnesses for HAC if results of a test for HAC were positive, 63 (31%) indicated they would treat such dogs for HAC only when the other disease was stabilized, 46 (23%) indicated they would treat such dogs for HAC only if the dogs had clinical signs of HAC (eg, pot-bellied appearance, alopecia), and 85 (42%) indicated they would retest for HAC once the other disease was stabilized. Other factors influencing the decision to treat, considered by < 5% of respondents each, were severity of the nonadrenal illness or the HAC, the presence of uncontrolled diabetes mellitus, and whether treatment of HAC would positively or negatively affect the other disease. In the specific case of diabetes mellitus, 167 of 196 (85%) respondents screened dogs with apparent insulin resistance for HAC even if no other clinical or laboratory data were consistent with HAC, whereas 27 (14%) did not, and 2 (1%) did sometimes.

Differentiating types of HAC—With regard to the LDDST, 132 of 206 (64%) respondents used the suppression pattern as a differentiating test, 72 (35%) did not, and 2 (1%) did sometimes. If the screening test did not also differentiate the underlying cause, 88 of 202 (44%) respondents indicated they would perform a differentiation test 100% of the time, 70 (35%) indicated they would 75 to 99% of the time, 18 (9%) indicated they would 50 to 74% of the time, 14 (7%) indicated they would 25 to 49% of the time, and 12 (6%) indicated they would < 24% of the time. With regards to the specific differentiation test, 58 of 204 (28%) respondents preferred the HDDST (0.1 mg of dexamethasone/kg, IV), 24 (12%) preferred the ultra high-dose dexamethasone suppression test (UHDDST; 1.0 mg of dexamethasone/kg, IV), 41 (20%) preferred measuring endogenous ACTH concentration, 1 (0.5%) preferred CT, 3 (1.5%) preferred abdominal radiography, 19 (9%) preferred abdominal ultrasonography, and 58 (28%) preferred to use a combination of tests.

If the initial differentiating test did not confirm the underlying cause of HAC, 22 of 201 (11%) respondents indicated they would initiate a trial of treatment with mitotane, 1 (0.5%) would initiate a trial of treatment with ketoconazole, 9 (4%) would repeat the initial differentiation test, 23 (11%) would perform an HDDST, 11 (5%) would perform a UHDDST, 37 (18%) would measure endogenous ACTH concentration, 2 (1%) would perform CT, 3 (1.5%) would perform MRI, 1 (0.5%) would perform abdominal radiography, and 29 (14%) would perform abdominal ultrasonography. Sixty (30%) respondents indicated they would perform other tests or a combination of tests, and 3 (1.5%) indicated the next step would vary depending on the case and owner. In interpreting the results of an HDDST, 102 of 170 (60%) respondents used an absolute value (eg, serum cortisol concentration < 30 nmol/L 4 or 8 hours after dexamethasone administration) as evidence of PDH, 48 (28%) used suppression to < 50% of the baseline value, and 20 (12%) used either criterion. If a dog was confirmed to have an AT, 54 of 203 (27%) respondents indicated they would attempt to biopsy the tumor, 139 (69%) would not, and 10 (5%) would sometimes.

Thirteen of 205 (6%) respondents indicated they use abdominal ultrasonography to differentiate PDH from HAC associated with an AT in 100% of cases, 38 (19%) did in 75 to 99% of cases, 38 (19%) did in 50 to 74% of cases, 28 (14%) did in 25 to 49% of cases, 73 (36%) did in 1 to 24% of cases, and 15 (7%) never did. There was a significant difference between internists and dermatologists with respect to use of ultrasonography to differentiate the underlying cause of HAC (**Table 3**).

One hundred thirty-six of 205 (66%) respondents had access to CT. Of these, 2 (1%) used CT in 50 to 74% of cases, 4 (3%) used it in 25 to 49% of cases, 81 (60%) used it in 1 to 24% of cases, and 49 (36%) never used it. For the 82 who used CT, the most common

Table 3—Numbers of internists and dermatologists responding to a survey on protocols for diagnosis of HAC in dogs who used abdominal ultrasonography to differentiate pituitary-dependent HAC from HAC secondary to an adrenal tumor

Percentage of cases	Internists	Dermatologists
100	12 (8)	1 (2)
75–99	36 (22)	2 (5)
50–74	28 (17)	8 (19)
25–49	22 (14)	6 (14)
1–24	53 (33)	20 (48)
0	10 (6)	5 (12)

Data are given as number of respondents (%).

indication was detection of a suspected pituitary macroadenoma (n = 57, 77%), but 8 (10%) used CT to assess pituitary size in all dogs with PDH, and 16 (20%) used CT to confirm a diagnosis of AT. Four respondents also used CT if the differentiation between PDH and HAC secondary to an AT was not clear following more conventional differentiating techniques, and 3 used it only as a prelude to definitive treatment, such as radiation therapy or hypophysectomy.

One hundred thirteen of 205 (55%) respondents had access to MRI. Of these, 1 (1%) used MRI in 25 to 49% of cases, 58 (51%) used it in 1 to 24% of cases, and 54 (48%) never used it. For the 59 who used MRI, the most common indication was detection of a suspected pituitary macroadenoma (n = 55, 79%), but 8 (11%) used MRI to assess pituitary size in all dogs with PDH, and 16 (23%) used it to confirm a diagnosis of AT. One respondent used MRI only if hypophysectomy was a potential treatment; 2 used it as a differentiating technique.

Discussion

In the present study, the number of dogs screened for HAC each year was significantly correlated with the number of dogs in which a diagnosis of HAC was made. This could suggest that the specialists who answered the survey screened dogs appropriately. Alternatively, it is possible that as the number of dogs that are screened increases, the number of false-positive test results also increases.

A common clinical dilemma is whether to screen a dog for HAC if that dog has few laboratory abnormalities (eg, high serum ALP activity) and no clinical signs consistent with the disease. Almost a third of specialists (31%) who responded to the present survey indicated they would not do so, whereas approximately a quarter (26%) indicated they would. The remaining specialists would consider doing so on the basis of a number of factors, including the owners' wishes, cost of testing, and the magnitude and duration of the increase in serum ALP activity. Interestingly, the willingness to screen for HAC in such dogs increased with the number of cases diagnosed per year. This may suggest that HAC is likely to be diagnosed with more aggressive testing or, alternatively, that more testing leads to a false-positive diagnosis. However, only 31% of specialists routinely treat dogs with few or clinical signs if tests for HAC are positive,[15] so a willingness to test for HAC does not equate with a willingness to treat.

Conversely, if serum ALP activity is within reference limits, 9% of specialists automatically rule out HAC as a possible diagnosis. However, although a normal serum ALP activity makes a diagnosis of HAC unlikely, it is not impossible to have a normal serum ALP activity in a dog with HAC.[16,17]

Overall, the LDDST appeared to be the single screening test preferred by most specialists who responded to the present survey. The high sensitivity of the LDDST[2] and the possibility that this test can differentiate the underlying cause of HAC[12] were cited by 48 and 37%, respectively, of respondents as reasons for preferring the LDDST. Combining published results of using the LDDST in 673 dogs with PDH or HAC secondary to an AT,[1,2,4,12,14,18-26] we estimate that the overall sensitivity is 95.1%. On the other hand, combining published results of using the ACTH stimulation test in 348 dogs,[1-3,5,14,20,22-28] we estimate that the overall sensitivity is 80.2%. For dogs with PDH, the sensitivity of ACTH stimulation testing is 87.4%,[14,22-24] whereas for dogs with an AT, the sensitivity is 61.3%.[3,14,28]

At times, a screening test different than the one normally preferred may be used. Reasons for choosing a different test when assessing dogs with no or few clinical signs of HAC were not solicited. However, a personal preference to use a test with high sensitivity versus high specificity may account for the use of an alternative test in such a situation. If results of the initial screening test are positive for a dog with few clinical or laboratory abnormalities consistent with HAC, most specialists (69%) would perform a second test for confirmation. Most likely this reflects concerns about the limitations of each test and the chance for false-positive results. Without the evidence provided by routine physical examination, historical, or laboratory findings, extra confirmation is sought.

The importance of routine physical examination, historical, and laboratory findings in the diagnosis of HAC is confirmed by the fact that only 21% of the specialists who responded to the survey performed a second confirmatory screening test in dogs with several clinical or laboratory abnormalities consistent with HAC in which results of an initial screening test were positive. Furthermore, 83% performed another screening test if their clinical suspicion was high but results of the initial test were negative. Of those who used the ACTH stimulation test or the LDDST as their initial test, 94 and 78%, respectively, would perform a second screening test in such a situation. This difference may reflect the higher sensitivity of the LDDST, compared with the ACTH stimulation test. Because of the higher sensitivity of the LDDST, the chance that a dog with HAC would have negative LDDST results is lower than the chance that a dog with HAC would have negative ACTH stimulation test results.

In dogs with serious nonadrenal illness, the initial screening test of choice was the ACTH stimulation test for 35% of the specialists and the LDDST for 41%. Of those who might use a different test for dogs with nonadrenal illness, 37% normally chose the ACTH stimulation test and 47% the LDDST. The reason for preferring the LDDST or for changing from the ACTH stimulation test is unclear, as 1 study[2] indicated the ACTH stimulation test is the most specific test in dogs with nonadrenal illness.

Not all dogs with nonadrenal illness for which results of a screening test for HAC are positive will be treated, and the recognition of the possibility of false-positive test results in such dogs likely accounts for this. Approximately 42% of specialists will retest for HAC once the nonadrenal illness is stabilized or resolved. Hyperadrenocorticism is apparently a frequently considered cause of insulin resistance, as 85% of specialists screen for HAC when insulin resistance is suspected, even when no other clinical signs or laboratory data are consistent with HAC.

In general, measurement of serum activity of the corticosteroid-induced enzyme of ALP was not a highly preferred test. This probably is a reflection of the low specificity of this test when screening for HAC. As with total ALP activity, the activity associated with the corticosteroid-induced enzyme of ALP is high in most dogs with spontaneous HAC and in most dogs that have received exogenous corticosteroids. However, serum activity of the corticosteroid-induced enzyme of ALP may be high in dogs that have not been given exogenous corticosteroids and do not have HAC.[29-37] Indeed, dogs likely to be screened for HAC, such as those with diabetes mellitus or hypothyroidism and those given phenobarbital, can have high serum ALP activities in which > 50% of the total serum ALP activity is attributable to serum activity of the corticosteroid-induced enzyme of ALP.[30,31,33,37,38] Overall, the sensitivity of measuring serum activity of the corticosteroid-induced enzyme of ALP as a test for glucocorticoid exposure (eg, HAC or exogenous glucocorticoid administration) is approximately 95%, but the specificity may be as low as 18%.[33,38]

Most specialists (79%) in the present study perform a differentiation test in > 75% of dogs with positive screening test results to determine whether the underlying cause is PDH or HAC secondary to an AT. Likely, this is because of the important therapeutic and prognostic information gained by differentiating the underlying cause. If mitotane is used for treatment, dogs with AT should be given higher induction and maintenance dosages, and induction should continue for a longer period.[39,40] Also, the prognosis for dogs with PDH is better than the prognosis for dogs with an AT.[39,41] The importance placed on differentiating the underlying cause is further reflected by the fact that only 12% of respondents indicated they would start treatment if the distinction was not obtained with the initial differentiation test, whereas the remainder do further testing.

Approximately two-thirds of specialists used information provided by the LDDST for differentiation. Depending on results of the LDDST, it is possible to determine whether PDH is present; however, presence of an AT can never be confirmed.[12] If differentiation is not obtained with the screening test, a number of tests can be used, with the HDDST, the UHDDST, and measurement of endogenous ACTH concentration being the most common. Reasons for preference of a specific test were not asked in the survey.

When analyzing results of the HDDST, 60% of respondents indicated that they used an absolute value to determine whether suppression of the serum cortisol concentration was consistent with PDH, 28% used a relative value (< 50% of the baseline concentration), and 12% used either. Typically, suppression to < 50% of the baseline concentration is considered consistent with PDH.[12] Rarely, however, cortisol concentration can be suppressed by administration of high doses of dexamethasone to dogs with AT. Two such cases have been reported.[12] Equivocal results may occur when the baseline cortisol concentration is similar to the absolute value that indicates suppression and when concentration is suppressed to just 50% of the baseline value.

Abdominal ultrasonography was used more commonly by internists than dermatologists in the present study to differentiate PDH from HAC secondary to an AT. This probably reflects availability and experience, as internists may obtain training in ultrasonography during their residency training, whereas dermatologists are unlikely to do so. Interestingly, approximately a third of internists used ultrasonography in at least 75% of their cases, and another third did so in < 25% of their cases. Whether this reflects availability and experience or opinion about the specificity of ultrasonography is unknown. In dogs with PDH, bilateral adrenal gland enlargement may be evident during abdominal ultrasonography; however, only 86% of AT are seen. In dogs in which an AT is not evident, the affected adrenal gland may appear normal or may not be visualized. The adrenal gland may also simply appear enlarged.[42]

Even when CT or MRI was available, these imaging modalities were not used by a high percentage of specialists. The most common reason for their use was to confirm a suspicion of pituitary macroadenoma. Some specialists also used CT or MRI to visualize the adrenal glands, and 11 to 12% of specialists used CT or MRI in all dogs with PDH to assess tumor size, regardless of whether a macroadenoma was suspected. However, small pituitary tumors may not be apparent with or without contrast,[43,44] so absence of a detectable mass does not rule out PDH. The benefits of routine MRI of all dogs with PDH for a detectable mass have been considered.[22,23] However, even if a mass is present, there is no way to predict whether the mass will grow or become clinically apparent,[45] Therefore, the clinical benefit of screening with MRI is unknown.

[a]Available from authors on request.

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