Endocrine diagnostics: staying out of the grey zone

2. Interpreting adrenal tests

Carmel T. Mooney

There is no perfect test for diagnosing canine hyperadrenocorticism; none is totally reliable, and each is beset with frequent false-positive and false-negative results in varying proportions. In some highly suspicious cases, definitively diagnosing hyperadrenocorticism is difficult because test results are negative. However, more importantly, many with non-adrenal illness have positive test results. Complicating matters are the influences of differing aetiologies and prior treatment. Maximizing diagnostic performance is dependent on several factors.

- Increasing pre-test probability — the prevalence of hyperadrenocorticism in the population under test should be maximized to increase the positive predictive value. Specific indications for testing include compatible signalment, history and clinical signs (the greater the number of signs the higher the suspicion), or the presence of an adrenal mass, or pituitary macrotumour, or poorly controlled diabetes mellitus despite high doses of insulin, but after exclusion of other causes and treating ketoacidosis. Absence of biochemical or hematological changes or adrenal gland enlargement do not rule out hyperadrenocorticism. The presence of any biochemical or haematological abnormality, increased urine protein:creatinine ratio and hypertension by themselves are not indications to test for hyperadrenocorticism
- Understanding the limitations of the test — the diagnostic sensitivity and specificity of the tests vary depending on the test itself, the underlying cause (adrenocorticotrophic hormone (ACTH) dependent or independent), the presence or absence of significant non-adrenal illness, the environmental circumstances and the nature of the dog. These must be weighed up and considered in each individual case
- The presence of non-adrenal illness — testing for hyperadrenocorticism should be avoided if a known serious illness exists. Postponing testing until that illness is resolved or stabilized is recommended
- Concurrent medications — apart from the possible effect of glucocorticoid use on the hypothalamic–pituitary–adrenal axis, certain glucocorticoids such as prednisolone cross-react in cortisol assays.

In general terms the ACTH-response test is considered insensitive (particularly with functional adrenal tumours versus pituitary-dependent disease) but its high specificity improves its positive predictive value. Measurement of cortisol precursors increases the sensitivity of this test but

this is offset by a loss of diagnostic specificity. A bonus of this test is its ability to identify cortisol-precursor-producing adrenal tumours and to diagnose iatrogenic disease.

The low-dose dexamethasone suppression test is highly sensitive but poorly specific. This limits its value in assessing dogs that have non-adrenal illness. However, the positive predictive value of the test is influenced by the pattern of the results obtained: if cortisol suppression does not occur the positive predictive value is higher, partial suppression patterns support hyperadrenocorticism but escape and inverse patterns have the lowest positive predictive values. An advantage of the low-dose dexamethasone suppression test is its ability to diagnose pituitary-dependent disease in up to 60% of cases.

The urine cortisol:creatinine has a similar diagnostic performance to that of the low-dose dexamethasone suppression test.

KEY LEARNING OBJECTIVES

- Know the indications and contraindications for adrenal function tests
- Be able to select the most appropriate adrenal function tests in individual cases
- Interpret the results of adrenal function tests correctly

MULTIPLE CHOICE QUESTIONS

1. Which low-dose dexamethasone suppression result pattern has the highest positive predictive value?
 - (A) Escape
 - (B) Inverse
 - (C) Partial suppression
 - (D) No suppression
2. A dog is presented for polyuria and polydipsia and you want to rule out hyperadrenocorticism. What is the most appropriate test to use?
 - (A) ACTH-response test
 - (B) ACTH-response with measurement of 17-OH progesterone
 - (C) Low-dose dexamethasone suppression test
 - (D) Urine cortisol:creatinine ratio
3. A dog with polyuria and polydipsia, pot belly, flank alopecia and supportive clinicopathological abnormalities is tested for hyperadrenocorticism with the following results: pre and post ACTH cortisol: 215 and 767 nmol/l; pre and 3 and 8 hours after low-dose dexamethasone administration 190 nmol/l, <27.6 nmol/l and <27.6 nmol/l. How would you interpret these results?
 - (A) The positive ACTH-response test confirms a diagnosis of hyperadrenocorticism
 - (B) The negative low-dose dexamethasone suppression test rules out hyperadrenocorticism
 - (C) The positive ACTH-response test and negative low-dose dexamethasone suppression test indicate pituitary-dependent hyperadrenocorticism
 - (D) The discordant results make diagnosis impossible