Hyperadrenocorticism

Hyperadrenocorticism results from over-secretion of cortisol and is an important endocrine disorder of dogs, primarily seen in older dogs. Dynamic tests are the cornerstone of diagnosis, and these tests evaluate the stimulatory and negative feedback pathways which form the basis of normal cortisol homeostasis.

Low dose dexamethasone suppression test

Currently the LDDST is regarded as the best screening test for dogs with visible signs of hyperadrenocorticism. Sensitivity is reported to be in the region of 97%, with a negative predictive value of in excess of 95%. The LDDST would therefore be expected to be abnormal in almost all patients with hyperadrenocorticism and a normal test result would indicate a less than 5% chance of the patient having hyperadrenocorticism. Values for specificity (55-78%) and positive predictive value (63-82%) are lower and more variable, affected by both case selection (most importantly the presence of non-adrenal disease) and the pattern of response following dexamethasone suppression. Interpretation of abnormal results is thus dependent on a full clinical history, including any concurrent disease or medications the patient is receiving. Assessment of adrenocortical function by means of a LDDST is not advised in patients with obvious non-adrenal disease, including but not limited to pyrexia, icterus, vomiting, diarrhoea, dyspnoea, coughing and uncontrolled diabetes mellitus. Concurrent procedures such as imaging, grooming and vaccination should be avoided for the duration of the LDDST, as these have been shown to increase cortisol concentrations. Depending on the temperament of the patient, hospitalisation for the duration of the test may not be ideal.

Fasting for the duration of the test is not recommended. A small percentage of dogs with adrenal-dependent disease may demonstrate aberrant expression of non-ACTH receptors, including gastric inhibitory peptide receptors. In these patients, over-secretion of cortisol is associated with recent feeding and false negative results may be associated with fasting. To avoid sample lipaemia feeding of small amounts of low- fat food is ideal.

Protocol:

Obtain a basal sample of at least 1ml using a red top/plain tube. Label this tube as T=0hrs
Inject 0.01mg/kg intra-venously
Obtain a second sample of at least 1ml using a red top/ plain tube, 4 hours following dexamethasone injection. Label this tube as T=4hrs
Obtain a third sample of at least 1ml using a red top/ plain tube, 8 hours following dexamethasone injection. Label this tube as T=8hrs
Submit all three samples to the laboratory with a full clinical history
Avoid the use of SST and gel tubes.

ACTH stimulation test

The ACTH stimulation test is primarily used for monitoring patients receiving treatment for hyperadrenocorticism, or for identifying hypoadrenocorticism, and less commonly as a primary diagnostic test for hyperadrenocorticism. The sensitivity of the ACTH stimulation test (70-80%) is less than that of the LDDST (~97%) and it is therefore not considered the screening test of choice. An ACTH stimulation test may be a useful adjunct to diagnosis in patients with equivocal LDDST results, known non-adrenal disease, or iatrogenic hyperadrenocorticism. Sensitivity of the ACTH stimulation test is particularly poor for the diagnosis of adrenal tumours (~20%) and is not advised in patients with ultrasonographic findings suggesting an adrenal tumour.

As with the LDDST, chronic non-adrenal disease may result in false positive results and a full clinical history is important when interpreting results. Fasting for the duration of the test is not advised, to maximise identification of food-dependent hyperadrenocorticism (see comment under LDDST). Feeding of a small amount of low-fat food is ideal.

Protocol:

Obtain a basal sample of at least 1ml using a red top/plain tube. Label this tube as T=0hrs
Inject Synacthen®IV or IM according to the preparation being used. Synacthen® may be administered at a flat rate of 125ug for dogs under 5kg or 250ug for dogs over 5 kgs, or at 5ug/kg. See comment on dosage rates below*.
Obtain a basal sample of at least 1ml using a red top/plain tube 60 minutes following injection of Synacthen®. Label this tube as T=1hr
Submit both samples to the laboratory with a full clinical history
Avoid the use of SST and gel tubes.

*Various dosage rates are quoted in the literature and are all suitable for diagnosis and monitoring of adrenocortical disease. Clinicians are encouraged to be consistent with the dosage protocol used, particularly in patients being subjected to ongoing monitoring.

Urine cortisol creatinine ratio

Cortisol is excreted in the urine and measurement of the cortisol concentration in sample taken in the morning will reflect average cortisol secretion over the past few hours. Concurrent measurement of creatinine allows for standardisation relating to urine concentration. The specificity of the urine cortisol creatinine ratio for diagnosis of hyperadrenocorticism is poor with 75-80% of dogs with non-adrenal test returning positive results. Specificity is worse for samples collected in the clinic and wherever possible it is preferable that the sample is collected at home, first thing in the morning. The diagnostic utility of this test is primarily in the exclusion of hyperadrenocorticism, as patients with a normal UCCR have a very low probability of hyperadrenocorticism. This test is not recommended for monitoring patients receiving treatment for hyperadrenocorticism.

References:

BSAVA manual of Canine and Feline Clinical Pathology 3rd edition 2018
Galac S et al. Expression of receptors for LH, gastric inhibitory peptide and vasopressin in normal dogs and cortisol-secreting adrenocortical tumours in dogs. Domestic Animal Endocrinology 2010;39:63-75.
Bennaim M et al. Evaluation of individual low-dose dexamethasone suppression test patterns in naturally occurring hyperadrenocorticism in dogs. J Vet Int Med 2018;32:967-977.