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Measurement of hormones in cats: the science behind the numbers

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Introduction: Measurement of hormones and interpretation of endocrinological test results are more complex and challenging than measuring and interpreting the results of other routine biochemical analytes (e.g. urea, albumin). The methodologies employed for measuring hormones are, in their vast majority, immunoassays which were originally developed for measuring human hormones and have undergone validation for use in cats. The technically demanding nature of such methodologies is reflected by the very low number of available point-of-care tests for measuring hormones in comparison to the relatively high number of point-of-care and bench-top analysers available for performing routine biochemical analyses in general practice.

The most common endocrinopathies in feline clinical practice are hyperthyroidism and diabetes mellitus. Even on the rare occasions where two endocrinopathies are present in the same patient, hyperthyroidism and concurrent diabetes mellitus are most frequently diagnosed (Blois et al 2010). This lecture will focus on the hormones most commonly measured in general practice for the diagnosis of and monitoring treatment of these two endocrinopathies (T₄, free T₄, TSH, IGF-1).

HYPERTHYROIDISM

Serum total T₄: Almost 95% of hyperthyroid cats can be diagnosed by a single high total T₄ result. Practitioners should know which assay is used in their in-house or external commercial veterinary laboratory. Serum T₄ can be measured by i) a radioimmunoassay (RIA) (not commonly used any more), ii) automated immunoassays employed by commercial laboratories (e.g., Immulite®) and iii) an ELISA test kit or bench-top immunoassay analyser for in-house use (Kemppainen and Bitchfield 2006, Higgs et al 2014). Although the correlation of serum T₄ concentrations between all of these assay methods is generally good, the generated results cannot be used interchangeably and assay specific reference intervals should always be used. If a high serum T₄ value is generated by an in-house assay in a cat

without clinical signs of hyperthyroidism (especially without a palpable thyroid nodule) the test should be repeated in an external laboratory.

Serum total T₄ is the preferred screening test for hyperthyroidism but almost 10% of all hyperthyroid cats (and up to 40% of cats with early or mild hyperthyroidism) have serum T₄ results within (middle to top end) of the reference interval; the most common explanations are fluctuations of T₄ and/or concurrent severe non-thyroidal illness suppressing mildly increased values to the middle or top end of the reference interval. In such cases the next laboratory investigation is to repeat T₄ in two weeks, measure free T₄ or TSH, or perform thyroid function tests.

Serum free T₄ (fT₄): Serum fT₄ concentrations are commonly measured by equilibrium dialysis and are elevated in more than 98% of hyperthyroid cats. However, the specificity of this test is questionable as it has been reported that 20% -30% of sick euthyroid cats, with total T₄ values in the low end or below the reference interval, have increased fT₄ results. Recently, many commercial veterinary diagnostic laboratories started employing fT₄ assays which do not use equilibrium dialysis, as the importance of this analytical step and its diagnostic accuracy has been questioned after generating high numbers of false positive results. For this reason fT₄ should not be used as a single test for the diagnosis of hyperthyroidism but in combination with total T₄ and clinical findings.

Serum Thyroid Stimulating Hormone (TSH): TSH will be suppressed in early stages of hyperthyroidism before total T₄ values are increased. It has been shown that feline TSH can be measured by a widely available canine TSH chemiluminescence immunoassay as a feline specific assay has not been developed. It has been reported that the diagnostic specificity of this test is poor as up to 30% of older, euthyroid, cats can have undetectable serum TSH concentrations; this is because the low limit of the current canine immunoassay is not low enough to distinguish between the low-normal serum TSH in some euthyroid cats from the truly low (totally suppressed) concentrations of most hyperthyroid cats. However, measurement of TSH has a high sensitivity (98%) and can be used to rule-out the disease as a cat with a result within the reference interval is highly unlikely to have hyperthyroidism.

DIABETES MELLITUS

Serum total insulin-like growth factor-1 (IGF-1): Most practitioners perform measurement of IGF-1 as a screening test for acromegaly (hypersomatotropism) in diabetic cats as it has been suggested to be the underlying cause of diabetes mellitus in 24-32% of diabetic cats.

However, false-negative results can occur as hepatic IGF-1 production is dependent on sufficient portal insulin, which can be deficient in newly diagnosed diabetic cats. In contrast, increased concentrations of IGF-1 have been reported in non-acromegalic diabetic cats. Currently measurement of feline IGF-1 is performed using radioimmunoassays which have inherent disadvantages (radioactive substances, restricted access, relatively high costs, variable assay performance). Recently the validation of an easy-to use and economical IGF-1 ELISA revealed that this assay had a high diagnostic accuracy for detecting hypersomatotropism in diabetic cats (sensitivity 100%, specificity 88%) (Rosca et al 2014).

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