Endocrine diagnostics: staying out of the grey zone

1. Interpreting thyroid tests

Robert Shiel

Combined measurement of total thyroxine (T4) and canine thyroid-stimulating hormone (cTSH) concentrations is recommended as the initial test for canine hypothyroidism. Testing should not be performed in the face of severe non-thyroidal illness, or when animals are receiving drugs known to alter thyroid hormone concentrations, if possible. The combination of total T4 and cTSH has a sensitivity and specificity of approximately 75% and >90%, respectively. Approximately 25% of hypothyroid dogs have decreased total T4 and reference interval cTSH concentrations. In such cases, measurement of free T4 concentrations or thyroglobulin autoantibodies can be helpful. Free T4 has high specificity (>90%), provided dogs with severe non-thyroidal illness are not tested and an appropriate assay is used. Traditionally, free T4 by equilibrium dialysis has been the gold standard. This is because several analogue methods may actually measure a proportion of total T4 rather than the actual free hormone concentration.

Increased cTSH with reference interval total T4 concentrations is most consistent with subclinical (compensating) hypothyroidism. This pattern can also be seen rarely in clinical hypothyroid dogs when T4 autoantibodies interfere with measurement of total T4. The presence of clinical and clinicopathological abnormalities will increase suspicion of clinical disease, and the measurement of free T4 concentrations with an appropriate assay will allow confirmation of the diagnosis. Thyroglobulin autoantibodies concentrations should also be increased in dogs with T4 autoantibodies due to lymphocytic thyroiditis.

Clinical hypothyroidism is extremely unlikely in dogs with reference interval total T4 and cTSH concentrations. Thyroglobulin autoantibody concentrations may identify dogs with silent thyroiditis, which can be useful in breeding programmes.

Thyroid scintigraphy or TSH-stimulation testing can be used to confirm thyroid status in difficult cases. More recently, the use of basal and thyrotropin-releasing hormone (TRH)-stimulated growth hormone (GH) and TSH measurements has shown promise. Primary hypothyroidism is associated with increased TRH-stimulated GH secretion, reflecting pituitary thyrosomatotroph transdifferentiation.

In cats, increased total T4 concentrations confirm hyperthyroidism with high certainty provided that an appropriate assay and reference interval have been used. Total T4 has a sensitivity of approximately 90%. The remaining 10% of hyperthyroid cats usually have values within the upper half of the reference interval due to mild hyperthyroidism or concurrent non-thyroidal illness. A high reference interval total T4 is not expected in significant non-thyroidal illness, and in such cases, hyperthyroidism is

likely. In cats with mild disease, free T4 concentrations are more commonly increased. In human medicine, decreased concentrations of TSH are most commonly used to confirm hyperthyroidism. The canine TSH assay has been used in cats but cannot differentiate between normal and low concentrations. Therefore, values below the limit of detection can be seen in both euthyroid and hyperthyroid cats. By contrast, measurable TSH makes hyperthyroidism extremely unlikely. Measurement of TSH is also useful for diagnosis of hypothyroidism in cats.

KEY LEARNING OBJECTIVES

- Be able to interpret a range of thyroid test results in dogs and cats
- Understand factors complicating interpretation of test results
- Have a confident approach to advanced investigation of thyroid disease

MULTIPLE CHOICE QUESTIONS

1. What is the most likely cause of the following results in a dog with alopecia and suspected hypothyroidism: total T4 concentration 7.5 nmol/l (reference interval 15–50 nmol/l); free T4 concentration (equilibrium dialysis) 18 pmol/l (reference interval 7–40 pmol/l); cTSH concentration 0.1 ng/ml (reference interval <0.68 ng/ml)?
(A) Non-thyroidal illness
(B) Primary hypothyroidism
(C) Silent thyroiditis
(D) Subclinical hypothyroidism
2. What is the most likely cause of the following results in a 3-year-old dog with weight gain, lethargy and dermatological changes: total T4 concentration 57 nmol/l (reference interval 15–50 nmol/l); free T4 concentration (equilibrium dialysis) 4 pmol/l (reference interval 7–40 pmol/l); cTSH concentration 0.7 ng/ml (reference interval <0.68 ng/ml)?
(A) Hyperthyroidism caused by dietary thyroxine excess
(B) Hyperthyroidism caused by excessive TSH secretion
(C) Silent thyroiditis with concurrent non-thyroidal disease
(D) Hypothyroidism caused by lymphocytic thyroiditis
3. Hyperthyroidism is suspected in a 10-year-old cat presented for mild weight loss. A small left-sided goitre is palpable. There are no other signs of illness. Total T4 measurement is 48 nmol/l (reference interval 15–60 nmol/l). Haematology and biochemistry reveal mildly increased liver enzyme activities. What single test would be best to confirm the presence of hyperthyroidism?
(A) TSH measurement
(B) Free T4 measurement
(C) Total T3 measurement
(D) Free T3 measurement