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Diagnostic Tests for Hyperthyroidism in Cats

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The diagnosis of hyperthyroidism, one of the most common disorders affecting elderly cats, is usually straightforward and considered routine by most practitioners. Nowadays, however, most cats suffering from hyperthyroidism tend to be diagnosed earlier and at a milder stage of the disease than those cats diagnosed 10 to 25 years ago. There are, in fact, a growing number of cats with clinical signs of hyperthyroidism and palpably large thyroid glands whose baseline serum total thyroid hormone concentrations are within the normal or borderline range, making diagnosis problematic. This paper reviews the available tests used to confirm a diagnosis of hyperthyroidism in cats and discusses their overall usefulness.

KEYWORDS hyperthyroidism, diagnosis, thyroxine, triiodothyronine, free thyroxine, nonthyoidal illness, T3 suppression, TRH stimulation

The diagnosis of hyperthyroidism in cats is usually straightforward and considered routine by most small animal clinicians. However, although diagnosis in most cats is not problematic, some cats suspected of having hyperthyroidism can be difficult to diagnose. Many of these cats have early or mild hyperthyroidism and show only mild clinical signs, whereas others appear to have more severe clinical features of hyperthyroidism but also have another obvious (or not so obvious) concurrent disease. The finding of hyperthyroidism developing concurrently with a nonthyroidal disease is not surprising given the fact that many of these cats are elderly.

Diagnosis of hyperthyroidism *must* take into account a cat's signalment, history, physical examination findings, and routine laboratory findings, as well as results of specific thyroid function tests. Most cats with hyperthyroidism are middle- to old-aged, with only 5% of cats younger than 10 years of age at time of diagnosis.[1,2]Common clinical signs observed in hyperthyroid cats include weight loss, normal to increased appetite, hyperactivity, vomiting, diarrhea, polydipsia, and polyuria.[1-5] As hyperthyroidism has become more recognized, veterinarians are diagnosing more cats at an early stage of the disease, in some cases even before owners realize that their cats are ill; such cats with very mild hyperthyroidism may not have any obvious clinical signs or have only a single sign (eg, mild weight loss despite a good appetite).[4,6-8] In hyperthyroid cats with concurrent disease (eg, renal disease, hepatic disease, or neoplasia), weight loss usually remains a common clinical sign but may be accompanied by decreased rather than normal to increased appetite. In these cats, depression and weakness may also replace hyperexcitability or restlessness as dominant clinical features.

On physical examination, enlargement of one or both thyroid lobes can be detected in 80 to 90% of cats with hyperthyroidism, a finding that is *extremely* important in making the diagnosis.[1-5] Although the thyroid gland is not usually palpable in normal cats, the finding of enlargement of one or both thyroid lobes on physical examination cannot be equated with hyperthyroidism, because thyroid enlargement occasionally can be detected in cats without other clinical and laboratory evidence of the disease.[9,10] Although some of these cats may remain euthyroid (at least for prolonged periods of time), many cats with thyroid gland enlargement eventually develop clinical and biochemical signs of hyperthyroidism as the thyroid nodules continue to grow and begin to oversecrete thyroid hormone.[6-10] Other findings commonly found on physical examination of hyperthyroid cats include evidence of weight loss, tachycardia, cardiac murmurs, and hyperkinesis.[1-5] These signs may not be pronounced in cats with mild or early hyperthyroidism. In hyperthyroid cats with concurrent disease, other clinical signs caused by the second disease may predominate.

Diagnosis of hyperthyroidism in cats, especially when early and mild or when associated with concurrent nonthyroidal diseases, requires that the veterinarian have a solid understanding of thyroid function and the pituitary-thyroid axis. The understanding of these mechanisms has led to the development and increasing use of provocative thyroid function tests in veterinary medicine. This review highlights the available tests for hyperthyroidism in cats and their clinical applications.

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Resting Serum Tests

Serum Total Thyroid Hormone Concentrations

High basal serum total thyroid hormone concentrations (ie, thyroxine [T_4] and triiodothyronine [T_3]) are the biochemical hallmark of hyperthyroidism. The finding of high T_4 or T_3 concentrations is extremely specific for its diagnosis with no false-positive results reported.[1-5,11] Methods for their measurement are readily accessible, relatively cheap and do not involve specific sampling requirements. Radioimmunoassay (RIA) is the preferred method, but nonisotopic and automated techniques are becoming increasingly popular.[12-14] Generally, these methods correlate reasonably well with results of RIA analysis, but technique and laboratory specific reference ranges should always be used. Assays intended for human serum are acceptable but must be fully validated for use with cat serum and modified to allow for measurement of the lower circulating concentrations of hormone in this species.

The serum concentrations of total T_4 and T_3 are highly correlated in hyperthyroid cats, but measurement of total T_4 is preferred over T_3 because of its better diagnostic sensitivity.[1-5,11] Over 30% of hyperthyroid cats have serum total T_3 concentration within the reference range, whereas only 10% of all hyperthyroid cats have normal serum T_4 concentrations.[2,11] Most cats with normal total T_3 concentrations have early or mild hyperthyroidism and, accordingly, corresponding serum total T_4 concentrations are usually only just above the reference range in these cats. Therefore, is likely that the normal T_3 concentrations would increase into the thyrotoxic range in these cats if the disorder were allowed to progress untreated. A possible explanation for normal circulating T_3 concentrations in cats with mild hyperthyroidism is that is that, as thyroid hormone production begins to increase in hyperthyroid cats, there is a compensatory decrease in peripheral conversion of T_4 to the more active T_3. Overall, measurement of serum T_3 cannot be strongly recommended as a diagnostic test for hyperthyroidism in cats; however, if serum T_3 is determined, it should always be measured together with a total T_4 concentration.[2,11]

Most hyperthyroid cats exhibit persistently high circulating total T_4 concentrations, with values up to approximately 20 times the upper limit of the reference range. However, a significant proportion of hyperthyroid cats (approximately 10% of all cases and 40% of cases with mild hyperthyroidism) have serum total T_4 concentration within the reference range.[2,11] Such normal T_4 values are usually within the mid to high end of the reference range. Thus, although serum T_4 is the best single test used to diagnose hyperthyroidism in cats, the disease cannot be excluded by the finding of a single, normal total T_4 concentration alone.

The finding of normal serum thyroid hormone concentrations in cats with clinical signs suggestive of hyperthyroidism can be problematic. How can a cat develop clinical signs (albeit mild in many cases) of hyperthyroidism when serum thyroid hormone concentrations remain within normal range? Two explanations have be proposed to explain the findings of normal serum thyroid hormone concentrations in cats with hyperthyroidism: (1) fluctuation of T_4 and T_3 in and out of the normal range[15] and (2) suppression of high serum T_4 and T_3 concentrations into the normal range because of concurrent nonthyroidal illness.[11,16,17] Approximately 20 to 30% of hyperthyroid cats that have circulating total T_4 concentrations within the reference range limits have an identifiable concurrent illness, the remaining majority are usually classified as mild or early cases.[11,17]

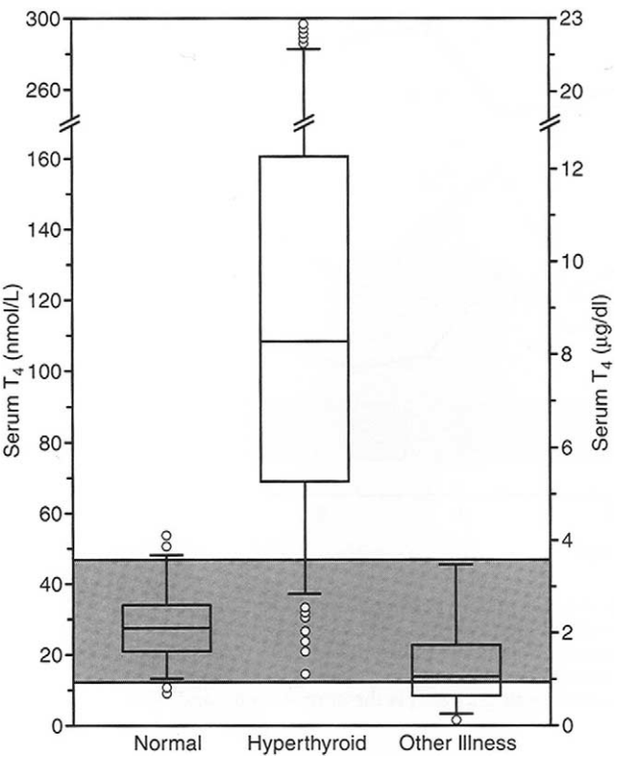

Figure 1 Serum T_4 and T_3 concentrations determined daily over a 15-day period in a cat with hyperthyroidism. Note the fluctuation in and out of the normal range for both serum T_4 and T_3 values. To convert serum T_4 concentrations from nmol/L to μg/dL, divide the given values by 12.87. To convert serum T_3 concentrations from nmol/L to ng/dL, divide the given values by 0.0154. (Used with permission from Peterson ME, Graves TK, Cavanagh I: Serum thyroid hormone concentrations fluctuate in cats with hyperthyroidism. J Vet Intern Med 1:142-146, 1987. © 1987 American College of Veterinary Internal Medicine.)

Thyroid hormone concentrations in cats with hyperthyroidism may fluctuate considerably over time.[3,12] In cats with thyroid hormone values well above the normal range, this fluctuation does not appear to be of great clinical or diagnostic significance. However, in cats with mild hyperthyroidism, the degree of serum T_4 and T_3 fluctuation that can occur—into the normal range in some cats (Fig. 1)—affirms that a diagnosis of hyperthyroidism cannot be excluded on the basis of the finding of a single normal to high-normal serum T_4 or T_3 result alone. In cats with clinical signs consistent with hyperthyroidism (and especially in cats with palpable thyroid nodules), more than one serum T_4 determination could be required to confirm a diagnosis. This fluctuation in and out of the normal range may explain, at least in part, the finding of normal or high-normal serum concentrations of T_4 and T_3 in some cats with clinical hyperthyroidism.

In hyperthyroid cats with concurrent nonthyroidal illness (eg, renal disease, diabetes mellitus, systemic neoplasia, pri-