Hyperthyroidism in cats
Part I: anatomy, physiology, pathophysiology, diagnosis and imaging

Hyperthyreoïdie bij katten
Deel I: anatomie, fysiologie, pathofysiologie, diagnose en beeldvorming

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Abstract

   In the first part of this review article, thyroid anatomy, physiology and pathophysiology are reviewed to continue more specifically on hyperthyroidism, the most common thyroid disorder in cats. The diagnostic work-up of this disorder is discussed with emphasis on thyroid gland imaging. Scintigraphy is most commonly used and best suited to assess thyroid function, which will be discussed extensively in the second part of this review article. All other available imaging modalities do not offer a functional assessment and are therefore of limited use in the diagnosis and evaluation of hyperthyroidism.

SAMENVATTING

   In het eerste deel van dit overzichtsartikel worden de schildklieranatomie, fysiologie en patho-fysiologie bij katten besproken. Vervolgens wordt de nadruk gelegd op hyperthyreoïdie, de meest voorkomende schildkliergerelateerde aandoening bij katten. De diagnosestelling wordt verder besproken met nadruk op de medische beeldvorming. Scintigrafie is veruit de meest gebruikte en geschikte techniek om de schildklierfunctie te evalueren. Daarop wordt in het tweede deel van dit overzichtsartikel dieper ingegaan. Andere beeldvormingsmodaliteiten bieden geen evaluatie van de schildklierfunctie en zijn daarom van minder belang voor de diagnose en evaluatie van hyperthyreoïdie.

THYROID GLAND ANATOMY

   The thyroid glands are two small elongated structures, located caudal to the larynx and lateral to the trachea on each side (Figures 1 and 2). Ventrally, they are covered by the sternothyroid muscle and laterally by the sternocephalic and sternohyoid muscles. The recurrent laryngeal nerve passes over their dorsal aspect. The size of a single lobe in cats is approximately 2 cm in length and 0.3 cm in width. The size of the gland can vary depending on factors such as the dietary iodine content. In case of iodine deficiency for example, the thyroid gland will increase in size (Dyce et al., 2010a; Dyce et al., 2010b). The presence of accessory, also called ectopic thyroid tissue, is not uncommon. This can occur in any location from the larynx along the trachea, at the level of the thoracic inlet or along the thoracic part of the descending aorta until the level of the diaphragm. An epithelial outgrowth from the pharyngeal floor gives rise to the thyroidal primordium, which is closely associated to the aortic sac during development. The thyroidal primordium will divide itself in two parts during development, expand laterally, and form the two separate thyroid lobes. At the same time, a migration from the region of origin at the tongue base towards its normal cervical position will take place. Little islets of thyroid cells can separate from the thyroidal primordium and become incorporated in developing structures of the thorax and brachial arch region due to this close relationship with the developing aortic sac. These islets will then form foci of ectopic thyroid tissue (Capen, 2007; Lynn et al., 2009; Dyce et al., 2010a; Dyce et al., 2010b; De Felice and Di Lauro, 2011; Peterson and Broome, 2015).

   Each thyroid lobe is vascularized by a cranial thyroid artery, branching from the common carotid artery at the level of the larynx. Venous drainage occurs by cranial and caudal thyroid veins, draining into the internal jugular veins or into the larger veins at the level of the thoracic inlet. Lymphatic drainage is provided by the deep cranial cervical lymph nodes. Nervous in-
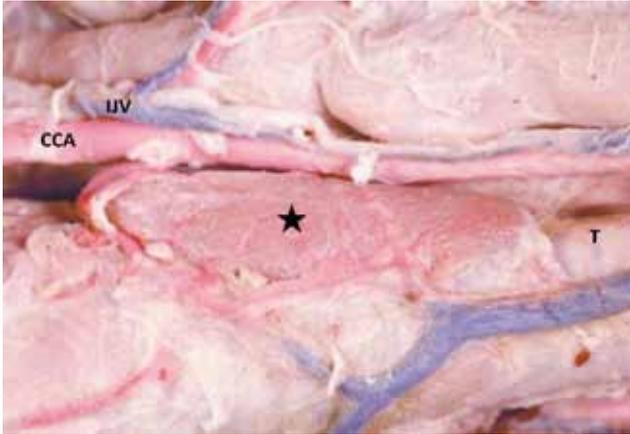
Figure 1. Anatomical image of a feline thyroid gland (Star : thyroid gland ; IJV : internal jugular vein; CCA: common carotid artery; T: trachea) (Sebastiani and Fishbeck, 2005).

nervation consists of both sympathetic origin, via the cranial cervical ganglia, and parasympathetic origin, via laryngeal branches of the vagus nerve. Their most important function is vasomotor control.

The thyroid glands are each associated with usually four parathyroid glands, two external to the thyroid gland cranially and two embedded within the thyroid capsule or thyroidal parenchyma caudally. In cats, the cranial parathyroid gland can descend and locate itself near the caudal pole (Dyce et al., 2010a; Dyce et al., 2010b).

THYROID GLAND PHYSIOLOGY: SYNTHESIS AND SECRETION OF THYROID HORMONES

The process starts at the level of the intestinal tract where iodine is trapped and converted to iodide that is transported by the blood. At the level of the thyroid, the iodide ion (I-) will be extracted from the blood stream by the sodium iodide (Na+I-) symporters (NIS) of the thyroid follicular cells. The iodide ion is then oxidized to iodine (I2) by the peroxidase enzyme and tyrosine will be incorporated in thyroglobine, a glycoprotein produced by the thyroid follicular cells. The tyrosyl residues will then be attached to iodine to form monoiodotyrosine (MIT) and diiodotyrosine (DIT). These can be coupled with the help of the thyroperoxidase enzyme to form biologically active iodothyronines: tetraiodothyronine or thyroxine (T_4) and triiodothyronine (T_3). These molecules are stored outside the peripheral follicular cells, within the colloid, which forms the center of a thyroid follicle and where a large reserve can be stored. When these molecules return to the follicular cell lumen and fuse with lysosomes, T_4 and T_3 are cleaved from the thyroglobin and can be secreted into the blood stream. In the peripheral tissues, mainly the liver and kidneys, a large amount of T_4 is deiodinated to T_3, the more potent hormone (Capen, 2007; Klein, 2012b) (Figure 3).

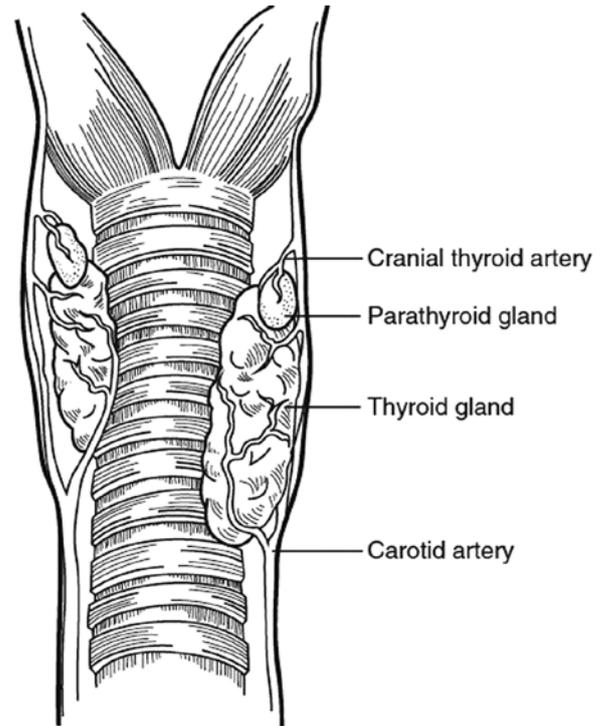Thyrotropin-releasing hormone (TRH), produced

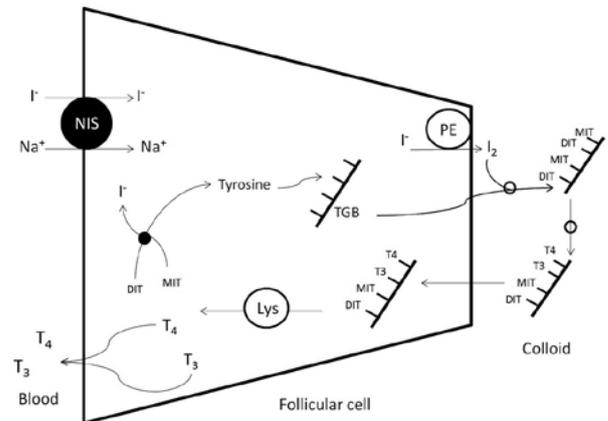**Figure 2. Drawing of the anatomy of the thyroid glands in a cat (Scott-Moncrieff, 2015).**

Figure 3. Schematic representation of the thyroid hormone synthesis. (NIS: sodium iodide symporter; TGB: thyroglobuline; PE/black circle: thyroid peroxidase enzyme; MIT: monoiodotyrosine; DIT: diiodotyrosine; Lys: lysosome).

by the hypothalamus, and thyroid stimulating hormone (TSH), produced by the adenohypophysis and released into the bloodstream in response to TRH, are the two controlling factors of thyroid hormone secretion. They interact together in a negative feedback system controlling serum hormone concentrations (hypothalamus-hypophysis-thyroid-axis). When the thyroid hormone concentration in the blood stream decreases, the hypothalamus is triggered to release TRH into the portal system of the adenohypophysis. TSH will then be secreted and stimulate the thyroid glands to increase the expression of the NIS and increase the

production and release of hormones. The reverse is also true, when the thyroid hormone concentration in the blood increases, the synthesis and release will be decreased (Capen, 2007; Klein, 2012a).

Thyroid hormones are responsible for the basal metabolic regulation. They work at all levels of the metabolism and are known to work generally catabolic. They cause an increased intestinal absorption of glucose and increased glycolysis and gluconeogenesis; an increase in the protein synthesis and lipid metabolism. At the same time, they will activate lipoprotein lipase and create an increase sensitivity of the adipose tissue to lipolysis, regulated by other hormones. They also increase the conversion of cholesterol into bile acids and other substances. All these processes increase the oxygen consumption and heat production of tissues and as a consequence the body temperature will increase. Other effects that can be observed are an increase in heart frequency, contraction force, cardiac output and finally blood flow; and an increase in neural transmission and cerebration. Thyroid hormones are also responsible for the development of the nervous system in young animals and normal growth and development in cooperation with growth hormone (Capen, 2007; Klein, 2012b).

FELINE HYPERTHYROIDISM

Hyperthyroidism refers to the overproduction of thyroid hormones from abnormally functioning thyroid tissue and is the most common endocrine disorder in middle to older aged feline patients. It was first described in the late seventies and early nineteen-eighties (Peterson et al., 1979; Holzworth et al., 1980, O'Brien et al., 1980; Jones et al., 1981; Watson et al., 1981). The prevalence of hyperthyroidism in cats has much increased since it was first reported. Increased awareness of the disease, environmental factors and better veterinary care most likely play an important role in this aspect. The overall prevalence varies geographically from 2.4% to 11.4%, with more specifically a prevalence of 8.7 to 11.4% in older cats. Only about 5% of hyperthyroid cats are younger than ten years at the time of diagnosis (Mooney, 2010; McLean et al., 2014, Stephens et al., 2014; Scott-Moncrieff, 2015).

Etiology

The underlying factors causing hyperthyroidism in cats are unknown. Multiple factors have been suggested to increase the risk of development of this disease, e.g. the consumption of mainly canned food, an indoor lifestyle, using cat litter, sleeping on the floor gathering dust enriched with chemicals that may be ingested during grooming, treatment with flea powders, exposure to herbicides and fertilizers, and other goitrogenic substances, e.g. present in soy. Other factors that might influence the disease development are the selenium and iodine content of the food (Gerber

et al., 1994; Capen, 2007; Mooney, 2010; Hill and Shaw, 2014; McLean et al., 2014; Peterson, 2014; Scott-Moncrieff, 2015; van Hoek et al., 2015). Some of these substances are believed to mimic T_4 and therefore stimulate cell division in the thyroid gland, increasing the risk of developing hyperthyroidism, although no conclusive evidence is available to support these theories.

In humans, two conditions associated with hyperthyroidism are known. Graves' disease is an autoimmune disorder where antibodies mimicking TSH bind to the TSH receptors. The role of antibodies in feline hyperthyroidism has been questioned but to this day, no evidence for a similar pathogenesis has been found (Nguyen et al., 2002; Mooney, 2010; Peterson, 2014). Gene mutations may also play a role in the pathogenesis (Peterson, 2014). Feline hyperthyroidism was found to resemble toxic nodular goiter in humans, also known as Plummer's disease, a progressive disease, due to the intrinsic growth of autonomously functioning thyroid nodules. The initiating cause to this growth however is unknown (Gerber et al., 1994; Peterson, 2014).

Feline hyperthyroidism in cats is most commonly secondary to functional (multi)nodular adenomatous hyperplasia (70 - 75%) or follicular cell adenomas (20 - 25%). A combination of both is also possible. More rarely, in about 1-3% of the cases, a thyroid carcinoma is present. Adenomas are mostly small, solid nodules that compress the remaining normal thyroid parenchyma. When these tumors become very large, necrosis, mineralization and cyst formation can occur (Phillips et al., 2003; Bailey and Page, 2007; Capen, 2007; Mooney, 2010; Peterson, 2014). These cystic adenomas can compress surrounding structures and may or may not be functional (Hofmeister et al., 2001; Phillips et al., 2003).

Thyroid carcinomas are often large tumors, with areas of necrosis, hemorrhage and possible mineralization. They can be locally invasive, and may metastasize to the lungs and lymph nodes (retropharyngeal and caudal cervical lymph nodes). It has been suggested that the prevalence of malignancy increases with the duration of the disease (Cook et al., 1993; Capen, 2007; Bailey and Page, 2007; Peterson et al., 2015a). The most common underlying disease, adenomatous hyperplasia, is commonly bilateral, in about 70% of cases and unilaterally in about 30% of hyperthyroid cats. Any of these underlying pathologies can also develop within ectopic tissue. A definitive diagnosis of the underlying disease can only be made by histopathology (Bailey and Page, 2007; Capen, 2007; Mooney, 2010).

Diagnosis of hyperthyroidism

The diagnostic work-up of hyperthyroidism is often based on a strong clinical suspicion. However, the disease may sometimes be accidentally recognized on annual health screenings. The diagnosis starts with an anamnesis and clinical examination and is completed

with a blood test and often the use of medical imaging, where scintigraphy stands out as the most important modality.

Clinical features

Clinical hyperthyroidism is the result of the increased production of thyroid hormones by thyroid pathology and the effect of these hormones throughout the body. As previously discussed, thyroid hormones have a broad range of action and consequently, clinical signs are variable and multisystemic. Cats are limited in their ability to metabolize and excrete T_4 with the bile compared to dogs. Therefore, they will show clinical signs more easily, even with small increases in thyroid hormone concentrations (Capen, 2007).

Hyperthyroidism is a disease typically seen in middle-aged to older cats. A large age range has been reported, from 2 to 23 years, with an average age of 12 – 13 years. A case of juvenile hyperthyroidism was reported in an eight-month-old cat that had typical clinical signs accompanied by a palpable thyroid nodule and an increased serum T_4 and T_3. The etiology for this early occurrence of hyperthyroidism could not be explained. There is no sex predilection for the disease; but regarding breed, some authors have reported an influence, with purebred cats and more specifically Himalayan and Siamese cats to have a decreased risk of developing hyperthyroidism (Gordon et al., 2003; Mooney, 2010; Klein, 2012b; Peterson and Broome, 2015). In a recent study, it has been described that the prevalence of different aspects of hyperthyroidism increases with duration of the disease: an increased serum total T_4 and T/S ratio; larger thyroid mass volumes; an increased number of patients with multifocal disease and intrathoracic masses; as well as an increased risk for suspected malignancy has been observed in patients that had been diagnosed for the longest time (Peterson et al., 2015a).

The most important clinical sign is weight loss while preserving a good to increased appetite. Other symptoms that have been described are hyperactivity, increased body temperature, aggressiveness, stress intolerance, altered behavior, muscle weakness/atrophy, hair coat changes, polyuria/polydipsia, systemic hypertension, polyphagia, vomiting, increased frequency of defecation with an increased volume of stool, diarrhea, tachycardia, systolic murmurs, cardiac arrhythmias, a mild form HCM with longstanding disease, tachypnea, panting, dyspnea, palpable cervical nodule(s) and papillary dilation (Holzworth et al., 1980; Bucknell, 2000; Capen, 2007; Mooney, 2010; Klein, 2012b; Peterson, 2014; Scott-Moncrieff, 2015). The atypical form of hyperthyroidism, also known as apathetic or masked hyperthyroidism, is associated with signs of depression and anorexia, often still accompanied by weight loss. It is important to keep in mind that not all hyperthyroid patients demonstrate the typical clinical presentation and signs may be subtle, especially in early stages (Bucknell,

2000, Mooney, 2010; Peterson, 2013b). An additional part of the clinical examination in cats, and especially when hyperthyroidism is suspected, is palpation of the thyroid glands. This is a simple and reliable diagnostic aid and a significant difference between normal and hyperthyroid cat palpation scores have been found in different studies (Norsworthy et al., 2002; Paepe et al., 2008; Boretti et al., 2009; Scott-Moncrieff, 2015).

It has to be borne in mind that thyroid nodules may also be an incidental finding, e.g. rare nonfunctional thyroid tumors, thyroid cysts, so finding a nodule on cervical palpation will not always translate itself in hyperthyroidism. Moreover, a cervical nodule can be of non-thyroidal origin, e.g. salivary gland disease, lymphadenopathy, a cervical abscess or granuloma (Capen, 2007; Peterson, 2013a; Peterson, 2013b; Scott-Moncrieff, 2015).

Blood Tests

Diagnosing hyperthyroidism usually starts with the measurement of the total T_4. An increased T_4 is indicative for hyperthyroidism. T_3 is less commonly measured but is also clearly increased in most hyperthyroid patients. Both are good markers for the disease; however, T_3 is not recommended as a screening test, since it is within the normal reference range in about 25 to 30% of the hyperthyroid cats and both T_4 and T_3 might be falsely low in animals with (concomitant) non-thyroidal illness (Capen, 2007; Shiel and Mooney, 2007; Mooney, 2010; Klein, 2012b; Peterson, 2013a; Peterson, 2013b; Peterson et al., 2015b).

Hyperthyroidism is a progressive disease that may sometimes be diagnosed in an early stage, when the clinical signs are still subtle and when T_4 measurements may still be within normal limits in a small number of cases. The opposite may also occur: a patient not showing any clinical signs can demonstrate a mildly elevated T_4 on a check-up blood test (Capen, 2007; Shiel and Mooney, 2007; Mooney, 2010; Peterson, 2013a; Peterson, 2013b; Peterson et al., 2015b). To confirm true hyperthyroidism in these patients, several options are available. First of all, a recheck T_4 measurement can be performed two to three weeks later, relying on the progressive nature of the disease, at the same time assuring that any potential concurrent disease has cured or has been treated. As hyperthyroid cats are usually older animals, it is important to consider the presence of non-thyroidal illness in these animals with normal or doubtful T_4 measurements. Moreover, when dealing with mild hyperthyroidism, it is known that the T_4 concentration may still fluctuate in and out of the normal reference range, making a final diagnosis challenging. Dynamic tests such as the T_3 suppression test can be performed as well. However, these tests are not often used. The T_3 suppression test has been found more sensitive for excluding hyperthyroidism rather than confirming the disease (Capen, 2007; Shiel and Mooney, 2007; Mooney, 2010; Peterson, 2013a; Peterson, 2013b; Peterson, 2014).

The free T_4 (fT_4) concentration may also be measured and may be of additional help in cases where the T_4 has not yet clearly increased or when the patient's clinical state is doubtful, as it is more sensitive than T_4. Since fT_4 increases whenever the T_4 has increased, it is of little use in the more straightforward cases of hyperthyroidism, and the cost of this analysis is much higher than for T_4. There is however the problem that fT_4 increases in animals with non-thyroidal illness and may even be increased in normal animals, potentially creating false positive diagnoses if this is the only measurement performed (Shiel and Mooney, 2007; Mooney, 2010; Klein, 2012b; Peterson, 2013a; Peterson, 2013b; Peterson and Broome, 2015; Peterson et al., 2015b). The method of measurement is also important for the determination of the fT_4 level, with the equilibrium dialysis being considered as the gold standard. This is an expensive technique, and is not performed in commercial laboratories. Other commercial techniques, like the modified equilibrium dialysis (MED) or analog radioimmunoassay (RIA), have shown to have an acceptable performance (Peterson, 2013a; Peterson, 2013b; Scott-Moncrieff, 2015).

TSH is commonly measured in human medicine for diagnosing hyperthyroidism. Unfortunately, to this day, no TSH assay has been made available for feline patients. The canine TSH assay may be used for cats but does not appear sensitive enough to differentiate all hyperthyroid cats from normal cats. As expected, the TSH measurement is low or unmeasurable on the canine TSH assay in hyperthyroid cats. However, low or undetectable measurements are also seen in euthyroid patients, or patients with non-thyroidal illness. Excluding hyperthyroidism may therefore be a more useful aspect of this test and TSH should not be used as a sole diagnostic parameter (Shiel and Mooney, 2007; Mooney, 2010; Peterson, 2013a; Peterson, 2013b; Peterson, 2014; Peterson et al., 2015b). In contrary to normal cats, TSH stimulation will not create a significant increase in T_4 or T_3 concentrations in hyperthyroid cats, as the cells responsible for the excess hormone concentration function autonomously, and the surrounding tissue is suppressed and atrophied. For patients in an early stage, the test is however not sensitive, and moreover, the high cost of recombinant human TSH that may be used for cats have made this test of little importance in practice (Stegeman et al., 2003; Capen, 2007; Shiel and Mooney, 2007; Mooney, 2010). Another test that may be used is the TRH stimulation test. However, it is again of limited specificity and the administration of TRH is commonly accompanied by side effects, such as vomiting, salivation, tachypnea and defecation (Shiel and Mooney, 2007; Mooney, 2010).

The most common changes on hematology or biochemistry profiles are a high packed cell volume (PCV), mean corpuscular volume (MCV), red blood cell count and hemoglobin concentration. Rarely, anemia may occur. Leukocytosis, neutrophilia, lymphopenia and eosinopenia can be observed, likely secondary to a stress response of increased catecholamines.

Increased liver enzymes, often very pronounced, are common: alanine aminotransferase (ALT), alkaline phosphatase (AP), lactate dehydrogenase (LDH), and aspartate aminotransferase (AST). A correlation between the concentration of AP and T_4 has been suggested. Liver function tests on the contrary are within normal limits and cholesterol can be decreased due to an increased clearance. While urea concentrations (BUN) may be increased or decreased, creatinine concentrations are low, possibly due to an overall loss of muscle mass in hyperthyroid cats and an increased glomerular filtration rate by the kidneys under the influence of increased thyroxine concentrations. Hyperphosphatemia, low calcium and increased levels of parathyroid hormone (PTH) are possible due to increased bone metabolism (Holzworth et al., 1980; Adams et al., 1997; Capen, 2007; Shiel and Mooney, 2007; Mooney, 2010; Klein, 2012b).

THYROID GLAND IMAGING

A small review of the literature on the imaging of thyroid glands in both normal and hyperthyroid cats is given. In contrary to scintigraphy, which will be discussed in the second part of this review article, radiography, CT, MRI or ultrasonography are of little value for the diagnosis of hyperthyroidism.

Although on rare occasions when patients undergo imaging for non-thyroid related disease, an abnormal thyroid gland may be noticed as an incidental finding, leading to further examination and possibly an early stage diagnosis of hyperthyroidism can be made.

Ultrasonography

Normal thyroid lobes are ellipsoid or fusiform in shape with a more rounded cranial and a pointed caudal pole on longitudinal plane, and as ovoid to triangular to polygonal in shape on the transverse plane. The lobes have a homogeneous appearance and are mildly hyperechoic compared to their surrounding musculature. They are outlined by a thin hyperechoic capsule (Wisner et al., 1994; Wisner et al., 2002; Zwingenberger and Wisner, 2008; Taeymans, 2011). Occasionally, the lobes show hypo- or hyperechoic foci or diffuse mottling of the parenchyma (Zwingenberger and Wisner, 2008).

The size and volume of a normal feline thyroid gland have been reported on ultrasonography. A single thyroid lobe measures approximately 2 cm in length, 0.2 cm in width and 0.3 cm in height. The normal mean total thyroid volume is 169 mm^3, with a mean thyroid lobe volume of 85 mm^3 (Wisner et al., 1994; Taeymans, 2011) and a significant increased volume was detected for thyroid glands in hyperthyroid cats (Wisner et al., 1994). In that study, another interesting finding was the fair correlation observed between the total thyroid volume and serum T_4 concentration of hyperthyroid cats.
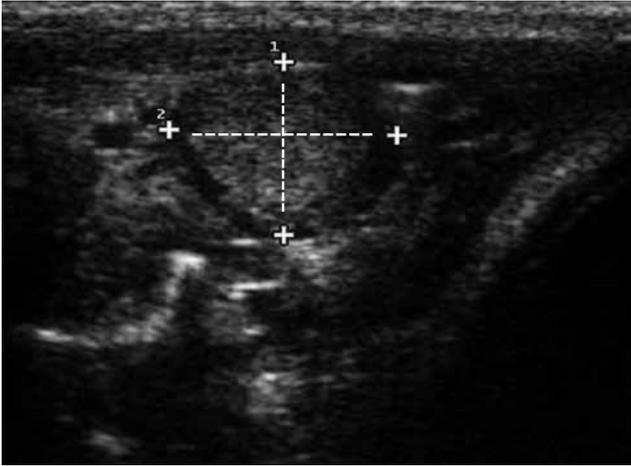
Figure 4. Transverse ultrasonographic image. A diffusely affected, mildly heterogeneous, enlarged right thyroid gland in a cat with hyperthyroidism. The calipers indicate the height (2) and width (1) of the lesion.

Figure 5. Lateral radiograph of the cervical area of a 15-year-old cat with hyperthyroidism and a severely enlarged thyroid gland (star). The enlarged thyroid gland is visualized as an ovoid, well-defined, soft tissue opacity ventral to the third and fourth cervical vertebrae. The lesion is creating a ventral displacement of the trachea and is well visualized thanks to the presence of a moderate amount of gas in the esophagus surrounding it. Wet hair artifacts are seen superimposed onto the ventral cervical region.

The parathyroid glands may be visualized on ultrasonography, adjacent to or embedded within the parenchyma. They are oval to round structures, up to 3.3 mm in diameter, hypoechoic to almost anechoic and may be difficult to differentiate from vessels, small cystic lesions or thyroid lobules. Their location and number may vary (Wisner et al., 2002; Zwingenberger and Wisner, 2008; Liles, 2010; Taeymans, 2011).

The use of ultrasonography in thyroid pathology has been described for the diagnosis of canine primary hypothyroidism and the differentiation from sick euthyroid syndrome, as well as for the diagnosis and work-up of thyroid cysts and neoplasia in both dogs and cats (Wisner et al., 2002; Phillips et al., 2003; Taeymans et al., 2007; Taeymans, 2011). The ultrasonographic appearance of adenomas or adenomatous hyperplasia causing hyperthyroidism in cats, may show different features (Figure 4). The lobe can be diffusely affected or show a discrete nodule deforming the normal outline. The lobe is usually increased in size, more rounded and has an increased vascularization. It becomes hypoechoic and heterogeneous. Anechoic areas may be observed, presenting necrosis or cystic lesions. In cats with a unilateral hyperthyroid adenoma or adenomatous hyperplasia, the other lobe is difficult to find or cannot be found at all (Wisner et al., 1994; Wisner et al., 2002; Zwingenberger and Wisner, 2008; Barberet et al., 2010; Mooney, 2010; Taeymans, 2011). Foci of mineralization have also been described in a cat with suspected benign disease (Barberet et al., 2010). On ultrasonography, thyroid carcinomas present as heterogeneous, hypoechoic masses with a variable delineation. Mineralization within these masses as well as invasion of adjacent structures has been described, and local lymph nodes should be checked for metastatic infiltration (Wisner et al., 2002; Zwingenberger and Wisner, 2008; Taeymans, 2011). Ectopic thyroid tissue can be present anywhere from the larynx until the level of the diaphragm and it is therefore important to always scan at least the entire cervical region (Capen, 2007; Lynn et al., 2009; Dyce et al., 2010a; Dyce et al., 2010b; De Felice and Di Lauro, 2011; Peterson and Broome, 2015). In a study comparing the diagnostic ability of ultrasonography and scintigraphy for hyperthyroidism in cats, a fair agreement of 85.7% was found in differentiating normal from abnormal thyroid lobes. Despite being an excellent imaging tool and permitting visualization of abnormal thyroid glands, it has been concluded however that ultrasonography cannot replace scintigraphy as a diagnostic tool for hyperthyroidism, especially for evaluating potential metastatic and ectopic lesions (Wisner et al., 1994). Ultrasonography has also been described in the follow-up of hyperthyroid cats after receiving radioiodine therapy to assess the visible changes that took place. At six months after therapy, the lobar volume had markedly decreased by approximately 75%, and there was a significant decrease of the rounded shape, the heterogeneity and the vascularization of the parenchyma (Barberet et al., 2010).

Radiography

Normal thyroid glands are not visible on radiography. In case of severe thyroid gland enlargement, they may become visible as a soft tissue mass effect in the cervical region or in the mediastinal region in case of ectopic thyroid tissue pathology (Phillips et al., 2003; Baines, 2008; Hayward et al., 2008) (Figure 5). However, radiography cannot differentiate these lesions from other soft tissue masses. When a thyroid carcinoma is suspected or confirmed, radiography can be used as a screening for pulmonary metastases (Figure 6). In about 50% of cats with hyperthyroidism,
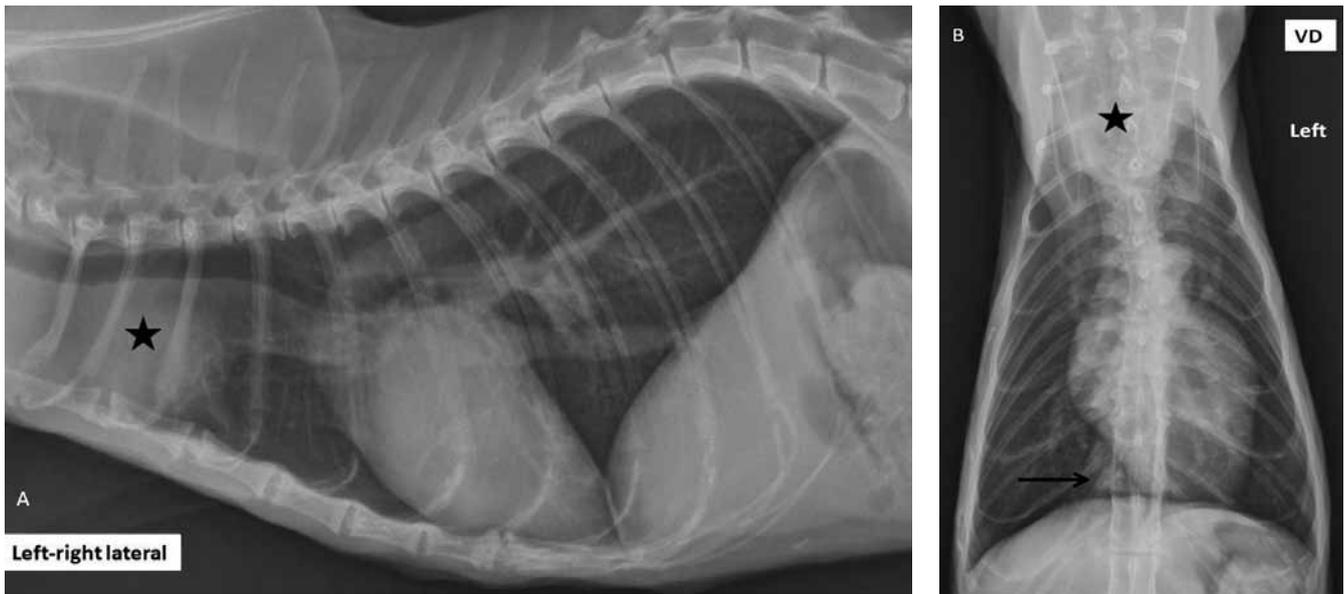
Figure 6. A. Left to right lateral projection of the thorax of a fourteen-year-old cat with hyperthyroidism. A large, ill-defined, rounded, soft tissue opacity (star) is seen in the cranial mediastinum at the level of the first – third intercostal space, creating a dorsal displacement of the trachea. B. A small pulmonary lesion is seen right to the midline on the ventrodorsal projection (VD), superimposed onto the caudal vena cava, and at the level of the seventh intercostal space on the lateral projection (arrow). On further examinations, these lesions were found to be compatible with a large thyroid carcinoma and pulmonary metastasis.

cardiomegaly can be observed on thoracic radiography, with or without secondary signs of heart failure. This is most commonly due to a certain degree of hypertrophic cardiomyopathy, or dilated cardiomyopathy in rare cases (Holzworth et al., 1980; Mooney, 2010).

Computed tomography

Due to the high iodine content of the thyroid glands, these structures have a characteristic hyperattenuating appearance compared to their surrounding tissues on computed tomography (CT). The Hounsfield units (HU) of a normal feline thyroid gland ranges around 123.2 HU on precontrast images, around 168.5 HU

immediately after intravenous contrast administration and around 132.1 HU with delayed contrast imaging (t = 8.6 ± 3.0 minutes). The thyroid glands are recognized as ovoid, homogeneous structures dorsolateral to the trachea, between the second and fourth cervical vertebrae (Drost et al., 2004; Drost et al., 2006; Taeymans and Schwarz, 2011) (Figure 7).

CT of the thyroid glands in hyperthyroid cats shows that the oval shape is usually maintained with smooth delineation, while being moderately increased in size. In case of bilateral disease, the most active lobe on scintigraphy is usually the largest one detected on CT. The affected lobes most commonly become isoattenuating to their surrounding soft tissues and show a heterogeneous appearance. Less commonly, minerali-
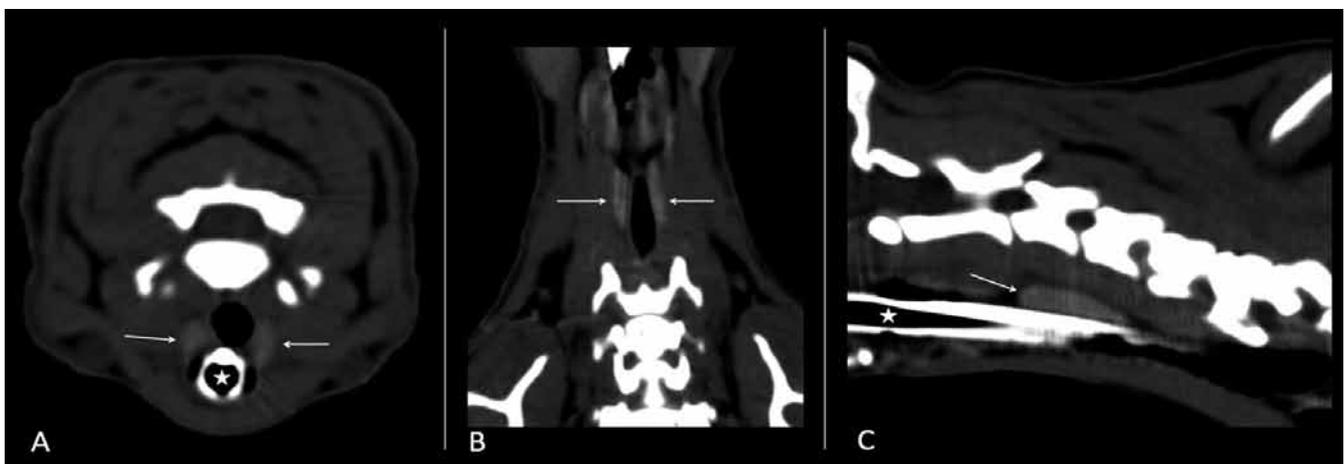

Figure 7. Precontrast transverse image (A), at the level of C3, and postcontrast dorsal (B) and sagittal plane (C) CT images of the thyroid glands of a normal cat (arrows). An endotracheal tube is present in the lumen of the trachea (star). Note the higher attenuation of the thyroid glands compared to the surrounding musculature.

zation within the parenchyma has also been observed. The loss of the normal strong attenuation has been proposed to be caused by an increased amount of follicular cells and interstitial tissue associated with a decrease in the normally high iodine concentration (Lautenschlaeger et al., 2013). This loss of normal thyroid gland hyperattenuation has also been reported in a rare case of hypothyroidism due to follicular hyperplasia in a five-year-old cat (Galgano et al., 2014). CT images of a hyperthyroid cat with a cystic thyroid lesion are illustrated in Figure 8.

Magnetic resonance imaging

The normal size and appearance of thyroid glands on MRI have been described in dogs but not yet in cats (Taeymans et al., 2008). One case of a cystic adenoma in a cat on MRI has been reported in the literature. The lesion was hyperintense on T_2-, proton density (PD)-, and T_2-fat suppressed weighted images, with a fluid line and decreased signal intensity in the dependent part of the mass. The wall had a signal intensity similar to the surrounding soft tissues. The other thyroid lobe in this cat had similar signal intensities to the large mass and was found to be a hyperplastic thyroid gland as well on the following scintigram (Hofmeister et al., 2001).

CONCLUSION

Hyperthyroidism is a commonly recognized disease in cats, with a variable but often rather typical clinical appearance. The exact etiology behind the disorder is unknown and is most likely multifactorial. Important factors of the diagnostic work-up include thyroid palpation and blood examination, with T_4 as the primary parameter to be measured. Non-functional imaging modalities are of little diagnostic aid, and should not be routinely performed when hyperthyroidism is suspected.
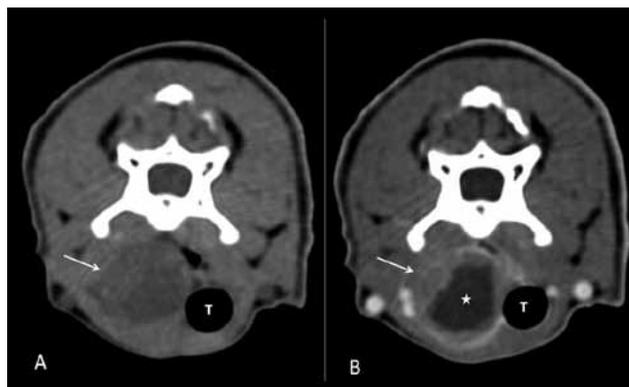

Figure 8. Pre- (A) and postcontrast (B), transverse CT images of a 15-year-old cat with hyperthyroidism. This is the same cat as in Figure 4. Note that the center of the lesion is non-contrast enhancing (star), suggesting a cystic thyroid lesion. This cystic nature was confirmed on ultrasonography (arrow: enlarged thyroid gland; T: trachea).

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