Original Article

jfms Journal of Feline Medicine and Surgery

Journal of Feline Medicine and Surgery
2017, Vol. 19(10) 1103–1109

DOI: 10.1177/1098612X16684408
journals.sagepub.com/home/jfms

This paper was handled and processed by the European Editorial Office (ISFM) for publication in *JFMS*

SAGE

Prevalence of and risk factors for feline hyperthyroidism in South Africa

Joanne L McLean[1,2], Remo G Lobetti[2], Carmel T Mooney[3], Peter N Thompson[4] and Johan P Schoeman[1]

Abstract

Objectives Hyperthyroidism is a disorder of older cats that may have a geographical variation in prevalence. Prevalence studies have not yet been performed in South Africa, a geographical area where hyperthyroidism in cats has recently been observed and where, reportedly, the incidence appears to be increasing. The purpose of this study was to determine the prevalence of feline hyperthyroidism in South Africa and to identify any potential risk factors. Further information on the worldwide prevalence and possible causative factors would increase our understanding of the aetiology of this disease and help identify any preventive measures.

Methods Serum total thyroxine (tT4) and canine thyroid-stimulating hormone (cTSH) were measured in 302 cats aged 9 years and older that were presented at various veterinary clinics throughout South Africa. In cats with equivocal tT4 and undetectable cTSH values, serum free thyroxine (fT4) was also measured. At the time of blood sampling a questionnaire was completed regarding vaccination history, internal and external parasite control, diet and environment.

Results Prevalence of hyperthyroidism (tT4 >50 nmol/l or tT4 between 30 and 50 nmol/l with TSH <0.03 ng/ml and fT4 >50 pmol/l) was 7% (95% confidence interval 4.4–10.4), with no significant difference between healthy (5%) and sick (8%) cats. Cats ⩾12 years of age (odds ratio [OR] 4.3, $P = 0.02$) and cats eating canned food (OR 2.1, $P = 0.1$) were more likely to be diagnosed with hyperthyroidism. No significant relationship between vaccinations, parasite control or indoor environment and hyperthyroidism was observed. Hyperthyroid cats were more likely to present with weight loss (OR 3.2, $P = 0.01$) and with a heart rate ⩾200 beats per min (OR 5, $P = 0.01$) than cats without the disease.

Conclusions and relevance Hyperthyroidism does not appear to be uncommon in the South African cat population. Risk factors for hyperthyroidism, specifically older age and eating canned food, were present in this as in other reported populations.

Accepted: 19 November 2016

Introduction

Feline hyperthyroidism is a multisystemic disorder arising from excess production of the active thyroid hormones (triiodothyronine and/or thyroxine [T4]) from an abnormally functioning thyroid gland.[1] Approximately 97–99% of cases result from benign nodular hyperplasia, adenomatous hyperplasia or adenoma of the thyroid gland.[2] The disease has been reported in cats between 4 months and 22 years of age with a mean age of 13 years.[3,4] Only 5% of hyperthyroid cats are younger than 10 years at time of diagnosis.[3] Clinically and histopathologically, the disease resembles toxic nodular goitre of humans, a disease of the elderly that is more common in iodine-deficient areas.[5]

[1]Department of Companion Animal Clinical Studies, University of Pretoria, South Africa
[2]Bryanston Veterinary Hospital, Johannesburg, South Africa
[3]University Veterinary Hospital, University College Dublin, Dublin, Ireland
[4]Department of Production Animal Studies, University of Pretoria, Pretoria, South Africa

Corresponding author:
Joanne L McLean BSc(Vet Biol), BVSc(Hons), Department of Companion Animal Clinical Studies, University of Pretoria, South Africa and Bryanston Veterinary Hospital, PO Box 67092, Bryanston, 2021, South Africa
Email: joanne@fuseprop.co.za

Feline hyperthyroidism was first described in 1979 and 1980 in New York and Boston.[6,7] Since these initial descriptions, several studies have documented a steady, yet marked increase in the prevalence of the disease in the cat population over time worldwide.[5,8,9] This disorder is now not only recognised as the most common endocrinopathy of the cat, but as one of the more frequently diagnosed disorders in small animal practice within North America, Western Europe, Australia, New Zealand and Japan.[1,10,11]

Several epidemiological studies suggest that hyperthyroidism is more common in countries such as North America, the UK and Germany but less common in countries such as Hong Kong and those in Scandinavia. However, it is difficult to compare directly the results of these studies because of marked differences in inclusion and exclusion criteria. Thus, definitive evidence of true geographical variation is generally lacking.[12] In one study, the incidence of hyperthyroidism in cats over 9 years of age was compared between veterinary clinics in the UK and in Spain over a 3 year period.[13] Both had a similar prevalence of cats aged over 9 years of age (16.4% and 20.1%, respectively), but there was a significant difference in incidence rates in the UK (11.9%) vs those in Spain (1.5%). The hospital prevalence among cats over 8 years of age in an urban population in Germany was noted as 11.4% in a 2006 study,[14] while a Portuguese study in 2014 found a prevalence of 9% in cats over the age of 10 years.[15] In Japan, a prevalence of 8.9% was reported in cats older than 9 years;[16] in Hong Kong, a prevalence of 3.9% was found in cats over 10 years of age;[17] a prevalence of 6% in apparently healthy cats over 9 years of age was reported in the UK;[18] while a more recent UK study reported a prevalence of 8.7% in cats over 10 years of age presenting to primary-care veterinary practices.[17] In a 2013 Irish study, a prevalence of 21% was reported in cats over 10 years of age presenting to private veterinary clinics in the greater Dublin area,[19] while a 2014 Polish study reported a prevalence of 20.4% in cats over 7 years of age from Warsaw.[20]

Despite its increasing frequency, the aetiology and underlying pathogenesis of the disorder is not known. Many of the epidemiological studies investigating prevalence have also attempted to identify potential risk factors for feline hyperthyroidism.[5,8,10,21–24] It has been postulated that immunological, infectious, nutritional (eg, iodine), environmental (eg, toxins or goitrogens) or genetic factors may interact to cause pathological changes within the thyroid gland eventually progressing to hyperthyroidism. Genetic or hereditary factors, nutritional component(s) in cat food leading to metabolic thyroid dysfunction or thyroid-disrupting compounds introduced into the environment or diet are the potential risk factors that have been most closely investigated.[11] The risk factors identified include living indoors, being female, living in multi-cat households, having dental disease (independent of age), being exposed to topical flea preparations and pesticides, using cat litter (not linked to living indoors), consuming certain flavours of canned foods (fish or liver and giblet flavour) and being a non-purebred cat. However, all of the studies have consistently failed to identify these risk factors and thus their significance remains uncertain.[12] Nevertheless, a number of these studies have also identified a number of common factors, including increased risk with age, decreased risk in Siamese and Himalayan cats, and increased risk in cats that consume canned cat food, especially pop-top canned food.

As far as we are aware, no prevalence studies have yet been performed in South Africa, a geographical area in which hyperthyroidism in cats has relatively recently been observed and reported and the incidence of which appears, anecdotally, to be on the increase. The purpose of this study was to determine the prevalence of feline hyperthyroidism in South Africa and to identify potential risk factors associated with the disease in this geographical location. Further research into the worldwide prevalence, as well as presence of possible causative factors, would help to elucidate the cause and pathogenesis of this disease and could lead to preventative measures.

Materials and methods

Case selection

This analytical cross-sectional study was conducted in cats that were presented for either geriatric check-ups and routine vaccinations or various illnesses at five general veterinary practices throughout South Africa between February 2014 and June 2015. Cats were included in the study if they were 9 years of age or older and had resided solely in South Africa. Cats were excluded from the study if their demeanour precluded the collection of a blood sample, or if they had been treated with drugs that could potentially affect total T4 (tT4) and thyroid-stimulating hormone (TSH) concentrations such as methimazole, glucocorticoids, phenobarbitone and trimethoprim-potentiated sulfonamides. At the time of blood sampling a questionnaire was completed regarding the health status of the cat, vaccination history, internal and external parasite control, diet and environment. Consent for blood collection was obtained from the owners and ethical approval for the study was also applied for and granted by the animal ethics committee of the University of Pretoria.

Sample collection and analysis

Blood samples were collected by jugular venepuncture, transferred into plain tubes and couriered on the same day to the Johannesburg or Cape Town branches of IDEXX laboratories, South Africa, where they were centrifuged and the serum separated, aliquoted and stored at −20ºC.

On a monthly basis, batches of stored samples were couriered on ice to the clinical pathology laboratory at the Faculty of Veterinary Science, University of Pretoria, to be stored at −80ºC for later tT4 and canine thyroid-stimulating hormone (cTSH) batch analysis. A small batch of samples was also couriered from the University of Pretoria on dry ice to Nationwide Specialist Laboratories, Cambridge, UK, for serum free T4 (fT4) analysis.

Serum tT4 and cTSH concentrations were determined in all cats by use of a chemiluminescent competitive immunoassay (Immulite 1000 Canine Total T4; Siemens Medical Solutions Diagnostics) and a chemiluminescent immunometric assay (Immulite 1000 Canine TSH; Siemens Medical Solutions Diagnostics), respectively. The reference interval (RI) for tT4 was 14–50 nmol/l (1.09–3.9 µg/dl) and for cTSH 0–0.07 ng/ml (historical laboratory RIs). Serum fT4 concentrations were measured in cats with a serum tT4 concentration between 30 and 50 nmol/l and a serum cTSH concentration <0.03 ng/ml using equilibrium dialysis (Antech Diagnostics Inc Free T4 by Equilibrium Dialysis) with an RI of 10–50 pmol/l (historical laboratory RIs). All cats with a serum tT4 concentration >50 nmol/l or cats with a serum tT4 concentration between 30 and 50 nmol/l, a serum cTSH concentration <0.03 ng/ml and a serum fT4 concentration >50 pmol/l were classified as hyperthyroid.

Statistical analysis

The prevalence of hyperthyroidism, with exact binomial 95% confidence intervals (CIs), was calculated for all cats combined, for cats classified as healthy (no clinically significant disease identified) and for those classified as sick. Prevalence was compared between healthy and sick cats using a two-tailed Fisher's exact test.

Univariate associations between potential risk factors and hyperthyroidism were assessed using a two-tailed Fisher's exact test. Thereafter, all predictors were entered into a multiple logistic regression model to estimate their association with the odds of hyperthyroidism. Non-significant variables were eliminated until remaining variables were significant at $P \leq 0.1$. The fit of the final logistic regression model was assessed using the Hosmer Lemeshow goodness-of-fit test. Associations between clinical signs and hyperthyroidism were assessed on a univariate level using a two-tailed Fisher's exact test. All analyses were performed using STATA version 14.1. Statistical significance was set as $P \leq 0.1$.

Results

The study population consisted of a total of 302 cats, with the majority of cats being sampled at two private veterinary practices in the Gauteng province of South Africa, namely the Bryanston Veterinary Hospital and Specialist Centre in Johannesburg (220 cats) and the Florida Veterinary Hospital in Krugersdorp (52 cats). The remaining cats were sampled at private veterinary practices in the Western Cape and Kwa-Zulu Natal provinces of South Africa, namely the Tygerberg Animal Hospital in Cape Town (23 cats), the Hilton Veterinary Hospital (4 cats) and Westville Veterinary Hospital (three cats). Breeds represented included domestic shorthair (n = 201), domestic longhair (n = 29), Siamese and Siamese Crosses (n = 26), Persian and Persian crosses (n = 10), Burmese (n = 10), Balinese (n = 6), Maine Coon and Maine Coon crosses (n = 5), domestic medium hair (n = 4), Birman (n = 2), Chinchilla (n = 2), Norwegian Forest (n = 2) and one each of Abyssinian, British Blue, Ragdoll, Russian Blue and Somali. There were 161 females and 141 males, of which 265 were neutered. The median age of the cats was 12 years (range 9–24 years).

Of the 302 cats, 118 cats were considered healthy and presented either for annual vaccinations (51 cats) or for routine visits (67 cats), while 184 were presented for various illnesses and considered sick.

The values of the tT4 measurements ranged between 1.3 and >190 nmol/l with a mean concentration of 25.8 nmol/l and a median concentration of 26.5 nmol/l. Twenty cats had a tT4 value >50 nmol/l, while 47 cats had a tT4 value between 30 and 50 nml/l. Of the 47 cats with a tT4 value between 30 and 50 nmol/l, 21 had a cTSH value <0.03 ng/ml, of which only one cat had a fT4 value >50 pmol/l. Only one of the cats with a tT4 value >50 nmol/l had a cTSH value >0.03 ng/ml. In total 21 cats were diagnosed as being hyperthyroid. Of the 21 hyperthyroid cats, 95% had an undetectable cTSH.

The prevalence of hyperthyroidism within the study population was 7% (95% CI 4.4–10.0) with no significant difference in prevalence between healthy (5% [95% CI 1.9–11.0]) and sick (8% [95% CI 4.6–13.0]) cats. There were no statistically significant differences in prevalence of hyperthyroidism between male and female cats, between purebred vs non-purebred cats or between Siamese and non-Siamese cats (Table 1). No statistically significant relationships between vaccinations, parasite control or indoor environment and hyperthyroidism were observed.

Only age and the presence of canned food in the diet were retained in the final logistic regression model of risk factors (Table 2). Cats ⩾12 years of age (odds ratio [OR] 4.3 [95% CI 1.2–15.0]; $P = 0.02$) and cats with canned food in their diet (OR 2.1 [95% CI 0.8–5.4]; $P = 0.1$) were more likely to be diagnosed with hyperthyroidism.

Table 3 lists the frequency of the main clinical features in the hyperthyroid cats. Weight loss and vomiting were the most common findings, followed by tachypnoea, tachycardia, presence of a cardiac murmur and polyphagia. Clinical features typically associated with hyperthyroidism were only noted in 14/21 hyperthyroid cats and only two had a palpable goitre. The mean tT4 concentration in the group of hyperthyroid cats with clinical signs

Table 1 Univariate analysis of risk factors for hyperthyroidism (total thyroxine [tT4] >50 nmol/l or tT4 between 30 and 50 nmol/l with thyroid-stimulating hormone <0.03 ng/ml and free T4 >50 pmol/l)

			Hyperthyroid cats		
Variable	Category	N	n	%	*P* value*
Age (years)	9–11	121	3	3	0.03
	12–14	93	10	11	
	>14	88	8	9	
Sex	Female	161	13	8	0.50
	Male	141	8	6	
Breed	DSH	201	13	7	0.62
	DLH	29	4	14	
	Siamese/Siamese crosses	26	1	4	
	Persian/Persian crosses	10	0	0	
	Burmese	10	0	0	
	Balinese	6	1	17	
	Other breeds	20	2	10	
	Purebred	61	3	5	0.57
	Non-purebred	241	18	8	
	Siamese/Siamese crosses	26	1	4	1.00
	Other breeds	276	21	8	
Number of cats in household	1	94	8	9	0.78
	2	104	7	7	
	>2	104	6	6	
Vaccinated	Yes	270	20	7	0.72
	No	18	0	0	
	Not sure	14	1	7	
Dewormed	Yes	274	20	7	0.44
	No	18	0	0	
	Not sure	10	1	10	
Flea control	Yes	139	8	6	0.54
	No	162	13	8	
	Not sure	1	0	0	
Exclusively indoors	Yes	246	18	7	0.78
	No	56	3	5	
Canned food in diet	Yes	71	8	11	0.11
	No	231	13	6	
Hunter	Yes	120	8	7	1
	No	182	13	7	
Water	Tap (unboiled)	256	18	7	0.34
	Tap (boiled)	32	1	3	
	Mineral	14	2	14	

**P* value for two-tailed Fisher's exact test
DSH = domestic shorthair; DLH = domestic longhair

was 114 nmol/l (range 56–193 nmol/l), while in the group of hyperthyroid cats without clinical signs this value was 79 nmol/l (range 40.3–193 nmol/l). Univariable analysis for these clinical signs as predictors of hyperthyroidism demonstrated that hyperthyroid cats were more likely to present with weight loss (OR 3.2 [95% CI 1.2–8.9]; $P = 0.01$) and with a heart rate ⩾200 beats per min (bpm; OR 5 [95% CI 1.7–16.1]; $P = 0.01$) than cats without the disease (Table 4).

Discussion

This study showed that the prevalence of hyperthyroidism in older cats presenting to private veterinary clinics in South Africa was 7%. This is similar to the prevalence rates reported in older cat populations in Japan and Portugal,[15,16] higher than that reported in Hong Kong but less than that reported in the UK and Germany.[14,17] It is, however, difficult to make direct comparisons between the results of different prevalence studies

Table 2 Final logistic regression model of risk factors for hyperthyroidism (total thyroxine [tT4] >50 nmol/l or tT4 between 30 and 50 nmol/l with thyroid-stimulating hormone <0.03 ng/ml and free T4 >50 pmol/l)

Variable	Category	OR	95% CI	*P* value
Age (years)	<12*	1.00	–	–
	>12	4.31	1.24–15.12	0.02
Canned food in diet	No*	1.00	–	–
	Yes	2.10	0.82–5.36	0.1

*Reference category
OR = odds ratio; CI = confidence interval

Table 3 Presenting clinical features in 21 hyperthyroid cats

Finding	Number of cats
Weight loss	12
Vomiting	7
Tachypnoea	4
Tachycardia (≥240 bpm)	3
Polyphagia	3
Cardiac murmur	3
Diarrhoea	2
Palpable thyroid lobe	2

bpm = beats per minute

Table 4 Univariate analysis of clinical signs associated with hyperthyroidism (total thyroxine [tT4] >50 nmol/l or tT4 between 30 and 50 nmol/l with thyroid-stimulating hormone <0.03 ng/ml and free T4 >50 pmol/l)

			Hyperthyroid cats		
Variable	Category	N	n	%	*P* value*
Weight loss	Yes	95	12	13	0.013
	No	207	9	4	
Polyphagia	Yes	46	3	7	1.00
	No	256	18	7	
Heart rate (bpm)	<200	193	6	3	0.001
	200–240	99	12	12	
	>240	10	3	30	
Cardiac murmur	Yes	16	3	19	0.090
	No	286	18	6	
Respiratory rate and pattern	Normal	277	17	6	0.042
	Increased	23	3	13	
	Dyspnoeic	2	1	50	
Vomiting	Yes	75	7	9	0.431
	No	227	14	6	
Diarrhoea	Yes	12	2	17	0.199
	No	290	19	7	

**P* value for two-tailed Fisher's exact test
bpm = beats per minute

because of the different inclusion and exclusion criteria and study methods used. This result does, however, support some geographical variation in the prevalence of the disease worldwide and that this variation could reflect differences in dietary, environmental and/or genetic factors. What is interesting to note is that the disease in the South African cat population appears to be much more prevalent than anecdotally thought. This may be owing to lack of awareness of the disease in clinical practice or lack of recognition of clinical signs by South African veterinarians.

Unlike previous prevalence studies, in this study serum tT4 and cTSH was tested in all cats and fT4 tested in cats that had a serum tT4 between 30 and 50 nmol/l and a cTSH <0.03 ng/ml in an attempt to detect hyperthyroid cats with early or subclinical disease or hyperthyroid cats with severe concurrent non-thyroidal illness. The cTSH assay has been used in the diagnosis of feline hyperthyroidism with an RI of 0.03–0.15 ng/ml for older cats.[25] In patients with subclinical and occult hyperthyroidism, cTSH levels are often low or undetectable.[26] One study that evaluated the usefulness of cTSH as a diagnostic test for feline hyperthyroidism, using thyroid scintigraphy as the gold standard, concluded that measurement of serum cTSH concentration was a very sensitive, but non-specific, diagnostic test with approximately 98% of hyperthyroid cats having serum cTSH concentrations suppressed below the limit of quantification (<0.03 ng/ml).[27] Unfortunately, the current commercial cTSH assay cannot accurately measure concentrations low

enough to distinguish clearly between euthyroid cats and hyperthyroid cats with suppressed concentrations. Combining serum cTSH with T4 or fT4 concentrations lowered the test sensitivity of cTSH from 98% to 97% but markedly increased overall test specificity (from 69.9% to 98.8%). Interestingly, in our study 95% of the hyperthyroid cats had an undetectable cTSH.

There was no difference in this study in the prevalence of hyperthyroidism between cats that were considered healthy and those that were considered sick. This may suggest that the disease is currently under-diagnosed in South Africa and that its early manifestations are insidious and challenging to recognise because it is often confused with other diseases or normal ageing changes.

In this current study there was an increased risk of hyperthyroidism with increasing age, with cats older than 12 years of age being four times more likely to have the disease. This is consistent with previous studies,[10,17,24] and also is in agreement with the fact that feline hyperthyroidism is a disease of middle-aged-to-old cats. In this current study, there were more female (n = 13 [62%]) than male (n = 8 [38%]) cats with hyperthyroidism, but the difference was not statistically significant. Most previously published studies report no sex predilection for feline hyperthyroidism.[7,8,22,28] However, two separate studies reported a significantly higher prevalence of hyperthyroidism in female cats,[5,10] and significantly more affected male than female cats.[14]

Two previous epidemiological studies have shown that Siamese cats have a significantly lower risk of developing hyperthyroidism compared with other breeds,[8,22] and three studies have demonstrated a protective effect in purebred cats.[10,21,24] In our study there were more non-purebred cats (n = 18 [86%]) with hyperthyroidism than purebred cats (n =3 [14%]), as well as a lower proportion of Siamese and Siamese-cross cats with hyperthyroidism (n = 1 [5%]), than all other breeds (n = 20 [95%]). However, the differences were, again, not statistically significant.

The present study and four previous studies all identified an increased risk of hyperthyroidism associated with an increased proportion of canned cat food in the diet.[5,8,22,23] One study incriminated particular flavours of canned food (fish, liver and giblets),[23] and another incriminated cans with plastic linings and easy-open (pop-top) lids.[5] Biologically plausible explanations for an association between feeding canned foods, especially of certain flavours, and hyperthyroidism may relate to the iodine content of canned vs dry cat foods (although the role that iodine plays in development of the disease is still largely unknown),[29,30] or the presence in the canned food of thyroid disruptors such as bisphenol A, polybrominated diphenyl ethers or flavonoids.[31] However, all these nutritional causes and risk factors remain speculative and lifelong prospective longitudinal studies are needed to investigate properly the role nutritional risk factors have in the development of hyperthyroidism.[31]

In this study, clinical features typically associated with hyperthyroidism were only noted in 14/21 hyperthyroid cats and only two had a palpable goitre. Thus, 7/21 hyperthyroid cats showed no overt clinical signs, which could be ascribed to the presence of a mild or early form of the disease (mean tT4 concentration of 114 nmol/l in group of cats with clinical signs vs 79 nmol/l in group of cats without clinical signs), but could also be due to lack of awareness of the disease by practitioners in South Africa owing to their preconceived impression that the disease is not prevalent in the country. The lack of a palpable thyroid nodule in 19/21 hyperthyroid cats was unexpected and could either be due to inexperience of the veterinarians or lack of thyroid enlargement owing to an early or subclinical form of the disease. Despite the absence of recognisable clinical signs in some of the hyperthyroid cats, this study showed that hyperthyroidism should be considered in any older cat demonstrating weight loss or a heart rate ⩾200 bpm.

The present study had some limitations that need to be considered. The low prevalence of hyperthyroidism, combined with the limited sample size, made it difficult to compare the group of hyperthyroid cats with the non-hyperthyroid cats. Bias may have been present as the study only included cats that were brought to veterinary practices. Although this bias may have influenced the risk factors identified in the study, it most likely had very little bearing on the prevalence of the disease reported as the veterinarian is only interested in the probability of encountering the disease in private practice.

Conclusions

Feline hyperthyroidism appears to be a relatively common disease in older cats presenting to private veterinary clinics in South Africa. Hyperthyroidism needs to be considered in any older individual demonstrating weight loss or a heart rate ⩾200 bpm in this cat population. The risk factors for development of feline hyperthyroidism identified in South Africa's relatively isolated population of cats appear to be somewhat similar to those that have been identified elsewhere.

Acknowledgements This study would not have been possible without the cooperation of all the veterinarians and cat owners in the various parts of South Africa, to whom the authors are greatly indebted. Our gratitude is also extended to all the staff at IDEXX Laboratories, South Africa, who not only took care of preparing and freezing the samples, but also provided valuable support in transportation of the samples to the various laboratories.

Conflict of interest The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding Financial support was provided by the Waltham Foundation, Waltham Centre for Pet Nutrition, Waltham-on-the-Wolds, UK.

References

1 Mooney CT. **Hyperthyroidism**. In: Ettinger S and Feldman E (eds). Textbook of veterinary internal medicine: diseases of the dog and cat. 7th ed. Philiadelphia, PA: WB Saunders, 2010, pp 1761–1779.

2 Gunn-Moore D. **Feline endocrinopathies**. *Vet Clin North Am Small Anim Pract* 2005; 35: 171–210.

3 Peterson ME, Randolf JF and Mooney CT. **Endocrine disease**. In: Sherding RD (ed). The cat: diseases and clinical management. New York: Churchill Livingston, 1994, pp 1416–1452.

4 Gordan JM, Ehrhart E J, Sisson DD, et al. **Juvenile hyperthyroidism in a cat**. *J Am Anim Hosp Assoc* 2003; 39: 67–71.

5 Edinboro CH, Scott-Moncrieff JC, Janovitz E, et al. **Epidemiologic study of relationships between consumption of commercial canned food and risk of hyperthyroidism in cats**. *J Am Vet Med Assoc* 2004; 224: 879–886.

6 Holzworth J, Theran P and Carpenter JL. **Hyperthyroidism in the cat: ten cases**. *J Am Vet Med Assoc* 1980; 176: 345–353.

7 Peterson ME, Kintzer PP, Cavanagh PG, et al. **Feline hyperthyroidism: pretreatment clinical and laboratory evaluation of 131 cases**. *J Am Vet Med Assoc* 1981; 183: 103–110.

8 Scarlett JM, Moise NS and Ray IJ. **Feline hyperthyroidism: a descriptive and case control study**. *Prev Vet Med* 1998; 6: 295–309.

9 Kraft W and Buchler F. **Hyperthyroidism: incidence in the cat**. *Tierarztl Prax Ausg Klientiere Heimtiere* 1999; 27: 386–388.

10 Olczak J, Jones BR, Pfeiffer DU, et al. **Multivariate analysis of risk factors for feline hyperthyroidism in New Zealand**. *N Z Vet J* 2005; 53: 53–58.

11 Peterson ME and Ward CR. **Etiopathologic findings of hyperthyroidism in cats**. *Vet Clin North Am Small Anim Pract* 2007; 37: 633–645.

12 Sparkes A. **Where are we now? Historical and epidemiological aspects of feline hyperthyroidism**. Proceedings of the Global Symposium on Feline Hyperthyroidism: The Rise and Fall of Thyroxine; 2012 May 9–11; Barcelona, Spain. pp 5–8.

13 Wakeling J, Melian C and Font A. **Evidence for differing incidences of feline hyperthyroidism in London, UK and Spain**. Proceedings of the 15th ECVIM-CA Congress; 2005 September 1–3; Glasgow, UK. p 220.

14 Sassnau R. **Epidemiological investigation on the prevalence of feline hyperthyroidism in an urban population in Germany**. *Tierarztliche Praxis Kleintiere* 2006; 34: 450–457.

15 Horspool LJI and Dias Neves R. **Prevalence of hyperthyroidism in portugese cats**. Proceedings of the 24th ECVIM-CA Congress; 2014 September 4–6; Mainz, Germany. p 198.

16 Miyamoto Y, Miyata I and Kurobane K. **Prevalence of feline hyperthyroidism in Osaka and the Chugoku region**. *Jpn Vet Med Assoc* 2002; 55: 289–292.

17 Stephens MJ, O'Neill DG, Church DB, et al. **Feline hyperthyroidism reported in primary-care veterinary practices in England: prevalence, associated factors and spatial distribution**. *Vet Rec* 2014; 175: 458–462.

18 Wakeling J, Elliott J and Syme H. **Evaluation of predictors for the diagnosis of hyperthyroidism in cats**. *J Vet Inten Med* 2011; 25: 1057–1065.

19 Gallagher B and Mooney CT. **Prevalence and risk factors for hyperthyroidism in Irish cats from the greater Dublin area**. *J Vet Intern Med* 2013; 27: 689.

20 Gojska-Zygner O, Lechowski R and Zygner W. **Prevalence of feline hyperthyroidism in mature cats in urban population in Warsaw**. *Bull Vet Inst Pulawy* 2014; 58: 267–271.

21 De Wet CS, Thomson PN, Mooney CT, et al. **Prevalence of and risk factors for feline hyperthyroidism in Hong Kong**. *J Feline Med Surg* 2009; 11: 315–321.

22 Kass PH, Peterson ME, Levy JK, et al. **Evaluation of environmental, nutritional and host factors in cats with hyperthyroidism**. *J Vet Intern Med* 1999; 13: 323–329.

23 Martin KM, Rossing MA, Ryland LM, et al. **Evaluation of dietary and environmental risk factors for hyperthyroidism in cats**. *J Am Vet Med Assoc* 2000; 217: 853–856.

24 Wakeling J, Everard A, Brodbel D, et al. **Risk factors for feline hyperthyroidism in the UK**. *J Small Anim Pract* 2009; 50: 406–414.

25 Wakeling JM, Moore K, Elliott J, et al. **Diagnosis of hyperthyroidism in cats with mild chronic kidney disease**. *J Small Anim Pract* 2008; 49: 287–294.

26 Wakeling J, Smith K, Scase T, et al. **Subclinical hyperthyroidism in cats: a spontaneous model of subclinical toxic nodular goiter in humans?** *Thyroid* 2007; 17: 1201–1209.

27 Peterson ME, Guterl JN, Nichols R, et al. **Evaluation of serum thyroid-stimulating hormone concentration as a diagnostic test for hyperthyroidism in cats**. *J Vet Intern Med* 2015; 29: 1327–1334.

28 Broussard JD, Peterson ME and Fox PR. **Changes in clinical and laboratory findings in cats with hyperthyroidism from 1983 to 1993**. *J Am Vet Med Assoc* 1995; 206: 302–305.

29 Johnson LA, Ford HC, Tarttelin MF, et al. **Iodine content of commercially-prepared cat foods**. *N Z Vet J* 1992; 40: 18–20.

30 Tarttelin MF, Johnson LA, Cooke RR, et al. **Serum free thyroxine levels respond inversely to changes in levels of dietary iodine in the domestic cat**. *N Z Vet J* 1992; 40: 66–68.

31 Van Hoek I, Hesta M and Biourge V. **A critical review of food-associated factors proposed in the etiology of feline hyperthyroidism**. *J Feline Med Surg* 2015; 17: 837–847.