Evaluation of dietary and environmental risk factors for hyperthyroidism in cats

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Objective—To identify dietary and environmental risk factors for hyperthyroidism in cats.

Design—Case-control study.

Animals—100 cats with hyperthyroidism and 163 control cats.

Procedure—Medical records were examined, and owners completed a mailed questionnaire. Data collected included information regarding demographic variables, environmental exposures, and diet, including preferred flavors of canned cat food.

Results—Case cats were significantly less likely to have been born recently than control cats. Housing; exposure to fertilizers, herbicides, or plant pesticides; regular use of flea products; and presence of a smoker in the home were not significantly associated with an increased risk of disease, but cats that preferred fish or liver and giblets flavors of canned cat food had an increased risk.

Conclusions and Clinical Relevance—Results suggest that cats that prefer to eat certain flavors of canned cat food may have a significantly increased risk of hyperthyroidism. (*J Am Vet Med Assoc* 2000; 217:853–856)

Hyperthyroidism was first reported as a clinical disorder in cats in 1979 and has since been recognized with increasing frequency. The increasing frequency with which the condition is diagnosed may be a result of heightened awareness of the disease among veterinary practitioners, an increase in the life span of cats (which provides a longer opportunity for development of the disease), or a true increase in disease incidence.[1] Hyperthyroidism is one of the most common endocrine disorders in cats and has become a leading cause of morbidity in middle-aged and older cats.[2,3]

If the increasing frequency of hyperthyroidism in cats is a result of a true increase in disease incidence, it is possible that the condition is of environmental origin and, therefore, preventable. The emergence of the disease throughout the United States within a relatively short period suggests that factors that contribute to development of hyperthyroidism occur nationwide.[3]

The first published case-control study of cats with hyperthyroidism[1] suggested that regular treatment with flea sprays or powders; living strictly indoors; exposure to lawn herbicides, fertilizers, or pesticides; and eating canned food were associated with an increased risk of hyperthyroidism.[1] The purpose of the study reported here was to further identify dietary and environmental risk factors for hyperthyroidism in cats.

Materials and Methods

Selection of case cats—Medical records of the Cat Clinic of Seattle were searched to identify cats in which serum **tetraiodothyronine** (T_4) concentration had been measured between June 1996 and June 1997. Cats were eligible for inclusion in the case group if serum T_4 concentration was > 4.5 µg/dl, the cat was ≥ 8 years old, and a clinical diagnosis of hyperthyroidism had been made. Cats included in the case group were classified as incident cases of hyperthyroidism if the initial diagnosis of hyperthyroidism had been made between June 1996 and June 1997 and as prevalent cases of hyperthyroidism if the initial diagnosis of hyperthyroidism had been made prior to June 1996.

Selection of control cats—Control cats were selected randomly from a computerized list of all cats examined at the Cat Clinic of Seattle in which serum T_4 concentration had been measured between June 1996 and June 1997. Cats were eligible for inclusion in the control group if serum T_4 concentration was ≤ 4.5 µg/dl, the cat was ≥ 8 years old, and the cat did not have any clinical signs of hyperthyroidism and hyperthyroidism had never been diagnosed.

Data collection—A questionnaire described as a study of feline health, diet, and household exposures was mailed to owners of case and control cats. A postcard reminder was sent to non-respondents 3 weeks after the initial mailing. The questionnaire contained questions relating to the following topics: demographic characteristics, medical conditions, household exposures, and diet, with emphasis on types and flavors of cat food consumed. In general, the questionnaire asked about exposures throughout the cat's lifetime up to the time the questionnaire was completed. Questions about the types (dry or canned) and sources (grocery or discount store, pet store, or veterinary clinic) of food consumed referred to the previous 5 years; questions about preferred canned cat food flavors (predominant ingredients) referred to current behavior.

Medical records of case and control cats included in the study were reviewed by a staff member of the Cat Clinic of Seattle, and information on demographic characteristics, medications, medical procedures, serum T_4 concentrations, and medical conditions was obtained.

Data analysis—**Odds ratios (OR)** and their corresponding 95% **confidence intervals (CI)** were calculated as esti-

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mates of relative risk. Two separate analyses were conducted. The first included all case cats as a single group; the second separated the case group into incident and prevalent cases. Sex and year of birth were examined as potentially confounding variables, and only year of birth was found to affect OR of the variables of interest. Therefore, all analyses were adjusted for year of birth. All analyses were performed with statistical software[a]; values of $P < 0.05$ were considered significant.

Results

Selection of case and control cats—One hundred case cats and 163 control cats were identified. Fifty-one of the case cats were classified as prevalent cases, and 46 were classified as incident cases. The remaining 3 cats could not be classified. Medical records for 98 (98%) of the case cats and 155 (95%) of the control cats were reviewed.

Questionnaire response rate—Owners of 80 (80%) case cats and 120 (74%) control cats returned completed questionnaires. Three (3%) case cats and 2 (1%) control cats had died, and owners of these cats chose not to complete the questionnaire. Owners of 6 (4%) control cats could not be contacted because of lack of a current address. The response rate for incident and prevalent cases was identical.

Risk factors—All cats were spayed or neutered (**Table 1**). Case cats were significantly less likely to have been born recently than control cats, but there was no difference between case and control cats in regard to the number of years owned by the current owner. Breed was not significantly associated with risk of hyperthyroidism.

Housing; exposure to fertilizers, herbicides, or plant pesticides; regular use of flea products (defined as collars, shampoo, dips, mousses, and powders); and presence of a smoker in the home were not significantly associated with an increased risk of disease (**Table 2**).

Cats that preferred fish or liver and giblets flavors of canned cat food had an increased risk of hyperthy-

Table 1—Demographic characteristics of cats with (case cats; n = 100) and without (control cats; 163) hyperthyroidism included in a case-control study of risk factors for the disease

			Incident cases (n = 46)*			Prevalent cases (n = 51)†		
Variable	No. of case cats (%)	No. of control cats (%)	OR	95% CI	No. of cases (%)	OR	95% CI	No. of cases (%)	OR	95% CI
Year of birth										
1976–1980	28 (28)	21 (13)	Ref	NA	11 (24)	Ref	NA	17 (33)	Ref	NA
1981–1984	62 (62)	66 (40)	0.7	0.4–1.4	30 (65)	0.9	0.4–2.0	30 (59)	0.6	0.3–1.2
1985–1988	10 (10)	76 (47)	0.1	0.0–0.2	5 (11)	0.1	0.0–0.4	4 (8)	0.1	0.0–0.2
Sex										
Male	40 (40)	77 (47)	Ref	NA	22 (48)	Ref	NA	18 (35)	Ref	NA
Female	60 (60)	86 (53)	1.3	0.8–2.3	24 (52)	0.9	0.5–1.9	33 (65)	1.8	0.9–3.7
Breed										
Mixed	82 (82)	119 (73)	Ref	NA	41 (89)	Ref	NA	39 (77)	Ref	NA
Siamese or Siamese-type	10 (10)	22 (14)	0.4	0.2–1.1	3 (7)	0.3	0.1–1.1	7 (14)	0.6	0.2–1.8
Other	8 (8)	22 (14)	0.5	0.2–1.2	2 (4)	0.2	0.1–1.1	5 (10)	0.7	0.2–2.0

*Cats in which a diagnosis of hyperthyroidism was made during the study period (June 1996 through June 1997). †Cats in which a diagnosis of hyperthyroidism was made prior to the study period.
OR = Odds ratio. CI = Confidence interval. Ref = Reference category. NA = Not applicable.

Table 2—Environmental exposures of cats with (n = 80) and without (120) hyperthyroidism

			Incident cases (n = 37)*			Prevalent cases (n = 40)†		
Variable	No. of case cats (%)	No. of control cats (%)	OR	95% CI	No. of cases (%)	OR	95% CI	No. of cases (%)	OR	95% CI
Housing										
Indoors only	14 (18)	36 (30)	Ref	NA	8 (22)	Ref	NA	6 (15)	Ref	NA
Rarely outdoors	18 (23)	17 (14)	1.9	0.7–5.1	9 (24)	1.5	0.5–5.0	8 (20)	1.8	0.5–6.5
Sometimes outdoors	40 (50)	59 (50)	1.8	0.8–3.8	16 (43)	1.2	0.4–3.2	22 (55)	2.1	0.8–5.8
Mostly outdoors	6 (8)	6 (5)	3.3	0.9–12.5	3 (8)	3.2	0.6–16.6	3 (8)	3.0	0.6–16.0
Not reported	2 (3)	1 (1)	NA	NA	1 (3)	NA	NA	1 (3)	NA	NA
Exposure to fertilizers, herbicides, or plant pesticides										
No	30 (38)	58 (48)	Ref	NA	15 (41)	Ref	NA	15 (38)	Ref	NA
Yes	24 (30)	31 (26)	1.8	0.8–3.7	9 (24)	1.5	0.5–4.1	14 (35)	1.8	0.7–4.3
Not reported	26 (33)	31 (26)	NA	NA	13 (35)	NA	NA	11 (28)	NA	NA
Regular use of flea products										
No	45 (56)	65 (54)	Ref	NA	23 (62)	Ref	NA	21 (53)	Ref	NA
Yes	33 (41)	51 (43)	0.8	0.4–1.5	13 (35)	0.7	0.3–1.5	18 (45)	0.9	0.4–2.0
Not reported	2 (3)	4 (3)	NA	NA	1 (3)	NA	NA	1 (3)	NA	NA
Smoker in the house										
No	60 (75)	88 (73)	Ref	NA	28 (76)	Ref	NA	30 (75)	Ref	NA
Yes	20 (25)	27 (23)	1.0	0.5–2.0	9 (24)	1.0	0.4–2.4	10 (25)	0.9	0.4–2.2
Not reported	0 (0)	5 (4)	NA	NA	0 (0)	NA	NA	0 (0)	NA	NA

Odds ratios were adjusted for year of birth. Not reported = Owner did not know or did not provide the information. *See* Table 1 for key.

Table 3—Preferred canned cat food flavors (primary ingredient) for cats with (n = 80) and without (120) hyperthyroidism

Canned cat food flavor	No. of case cats (%)	No. of control cats (%)	OR	95% CI	Incident cases (n = 37) No. of cases (%)	Incident cases (n = 37) OR	Incident cases (n = 37) 95% CI	Prevalent cases (n = 40) No. of cases (%)	Prevalent cases (n = 40) OR	Prevalent cases (n = 40) 95% CI
Fish										
No	35 (44)	72 (60)	Ref	NA	11 (30)	Ref	NA	22 (55)	Ref	NA
Yes	45 (56)	48 (40)	1.9	1.0–3.5	26 (70)	3.8	1.6–8.6	18 (45)	1.3	0.6–2.7
Tuna										
No	34 (43)	55 (46)	Ref	NA	14 (38)	Ref	NA	18 (45)	Ref	NA
Yes	46 (58)	65 (54)	1.1	0.6–2.0	23 (62)	1.4	0.6–3.1	22 (55)	1.0	0.5–2.2
Salmon										
No	43 (54)	76 (63)	Ref	NA	16 (43)	Ref	NA	25 (63)	Ref	NA
Yes	37 (46)	44 (37)	1.6	0.9–3.0	21 (57)	2.7	1.2–6.0	15 (38)	1.1	0.5–2.3
Trout										
No	60 (75)	98 (82)	Ref	NA	26 (70)	Ref	NA	32 (80)	Ref	NA
Yes	20 (25)	22 (18)	1.4	0.7–2.9	11 (30)	1.9	0.8–4.6	8 (20)	1.1	0.4–2.8
Poultry										
No	35 (44)	67 (56)	Ref	NA	18 (49)	Ref	NA	15 (38)	Ref	NA
Yes	45 (56)	53 (44)	1.5	0.8–2.7	19 (51)	1.2	0.5–2.6	25 (63)	1.9	0.9–4.1
Chicken										
No	36 (45)	51 (43)	Ref	NA	18 (49)	Ref	NA	16 (40)	Ref	NA
Yes	44 (55)	69 (58)	0.8	0.5–1.5	19 (51)	0.7	0.3–1.6	24 (60)	1.0	0.4–2.1
Turkey										
No	41 (51)	62 (52)	Ref	NA	21 (57)	Ref	NA	18 (45)	Ref	NA
Yes	39 (49)	58 (48)	1.0	0.5–1.8	16 (43)	0.7	0.3–1.6	22 (55)	1.2	0.6–2.6
Beef										
No	41 (51)	72 (60)	Ref	NA	18 (49)	Ref	NA	21 (53)	Ref	NA
Yes	39 (49)	48 (40)	1.3	0.7–2.4	19 (51)	1.4	0.6–3.0	19 (48)	1.1	0.5–2.4
Liver and giblets										
No	44 (55)	90 (75)	Ref	NA	19 (51)	Ref	NA	23 (58)	Ref	NA
Yes	36 (45)	30 (25)	2.4	1.3–4.6	18 (49)	2.7	1.2–6.1	17 (43)	2.0	0.9–4.3
Mixed fish and poultry										
No	52 (65)	88 (73)	Ref	NA	24 (65)	Ref	NA	26 (65)	Ref	NA
Yes	28 (35)	32 (27)	1.6	0.8–3.0	13 (35)	1.5	0.7–3.5	14 (35)	1.4	0.6–3.2
Mixed beef and poultry										
No	58 (73)	96 (80)	Ref	NA	25 (68)	Ref	NA	31 (78)	Ref	NA
Yes	22 (28)	24 (20)	1.5	0.8–3.1	12 (32)	2.0	0.9–4.8	9 (23)	1.0	0.4–2.5
Mixed poultry and giblets										
No	53 (66)	85 (71)	Ref	NA	23 (62)	Ref	NA	28 (70)	Ref	NA
Yes	27 (34)	35 (29)	1.1	0.6–2.1	14 (38)	1.3	0.6–2.9	12 (30)	0.8	0.3–1.8
Mixed unknown										
No	63 (79)	88 (73)	Ref	NA	27 (73)	Ref	NA	33 (83)	Ref	NA
Yes	17 (21)	32 (27)	0.7	0.3–1.4	10 (27)	1.0	0.4–2.3	7 (18)	0.5	0.2–1.4

Odds ratios were adjusted for year of birth. *See* Table 1 for key.

roidism (**Table 3**). In addition, cats classified as incident cases of hyperthyroidism that preferred salmon-flavored canned cat food had an increased risk of disease.

Discussion

The most common cause of hyperthyroidism in cats is functional thyroid adenomatous hyperplasia[4]; however, the pathogenesis of the adenomatous hyperplastic changes remains unclear. To date, only 1 study[5] has identified a promoter of spontaneous thyroid hyperplasia. Kittens fed an all-meat diet developed thyroid hyperplasia, which was attributed to the high protein content and deficiencies of calcium, vitamin A, and iodine.

Hyperthyroidism in cats most closely resembles toxic nodular goiter in humans, which is the most common cause of hyperthyroidism in humans.[3] Toxic nodular goiter commonly develops in old age and is caused by one or more hyperfunctioning adenomatous thyroid nodules.[6] It has been associated with a number of environmental causes, including deficiencies and excesses of dietary iodine, as well as exposure to environmental goitrogens (such as tobacco smoke and volatile hydrocarbons from fireplaces).[7]

Studies of the effect of excess iodine on the thyroid gland in humans may shed some light on the role dietary iodine plays in development of hyperthyroidism in cats. It appears that in people, autonomous nodules of the thyroid gland are a common feature of old age. These may cause hyperthyroidism, regardless of dietary iodine intake, but hyperthyroidism may develop sooner with high dietary iodine intake.[8] In 1 study,[9] small quantities of iodide (0.5 mg/day) administered to human patients with autonomous thyroid nodules induced hyperthyroidism.

A number of studies have evaluated the iodine content of cat foods.[10] In 1 study,[11] it was found that the concentration of iodine varied widely in commercial cat foods in New Zealand, and whereas some foods contained very small amounts, others contained amounts that exceeded the recommended amount for cats. It has been speculated that short-term feeding of cat food that varies widely in iodine content results in a dramatic thyroid response, but it is not clear whether such variation could lead to permanent thyroid disease and eventually hyperthyroidism.[3,12]

Another study[13] examined the nutrient content of 13 cat foods available in the United States. All but 1 of the cat food samples contained added iodine in various synthetic forms. Sources of this added iodine include a number of plant and animal materials, especially ocean

fish, as well as certain artificial food dyes that contain iodinated compounds. The recommended iodine concentration for the diet of adult cats varies from 0.14 to 3.0 mg/kg of dry diet.[13] The iodine concentration for a number of the cat foods in the study by Mumma et al[13] was about 10 times the recommended amount.

In the present study, cats that preferred to eat certain flavors of canned cat food (fish flavor or liver and giblets flavor) were found to have a significantly increased risk of hyperthyroidism, compared with cats that did not prefer to eat those flavors of cat food. Conceivably, cat foods labeled as fish flavored may have relatively high iodine concentrations, because ocean fish tend to be high in iodine content[14]; however, we did not observe an increased risk among cats that preferred tuna flavored cat food.

The present study had several limitations that need to be considered. The small size of the study and low prevalence of particular exposures of interest limited the precision of some results. Also, to the extent that dietary and other exposures may change after a diagnosis of hyperthyroidism, our findings for cats classified as prevalent cases of disease may inaccurately assess risk factors for this disease. Our findings are also limited by the accuracy with which cat owners were able to report the cat food flavor preferences of their cats. In general, such accuracy might be expected to be similar among owners of case and control cats, and the resulting misclassification of dietary exposures would thus be expected to reduce the strength of any associations observed. On the other hand, because owners were asked only to report their cats' current preferences, inaccuracy associated with owner recall should have been minimal.

In a previous case-control study involving 56 case cats and 117 control cats,[1] regular treatment with flea sprays or powders; living strictly indoors; exposure to lawn herbicides, fertilizers, or pesticides; and feeding canned food were identified as risk factors for hyperthyroidism. In the present study, however, type of housing; exposure to fertilizers, herbicides, or plant pesticides; and regular use of flea products were not found to significantly increase the risk of hyperthyroidism. Similarly, in another study,[15] housing; exposure to lawn fertilizers, herbicides, or pesticides; and regular use of flea powders and sprays were not associated with an increased risk of hyperthyroidism. Differences between results of these studies may be attributable to imprecision due to small sample size, inaccuracies in recall of relevant exposures, or chance.

In a previous study,[1] the risk of hyperthyroidism among Siamese cats was a tenth of the risk for non-Siamese cats; and in a second study,[15] risk for Siamese and Himalayan cats was reduced, compared with cats of other breeds. In the present study, a significant association with breed was not observed; however, the relative risks for Siamese and other purebred cats were low. Thus, our inability to detect a significant association between breed and hyperthyroidism may have been a reflection of the small sample size.

[a]Stata, version 5.0, Stata Corp, College Station, Tex.

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