UPDATE ON FELINE THYROID DISORDERS
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UPDATE ON THE PATHOGENESIS OF FELINE HYPERTHYROIDISM

Feline hyperthyroidism was first described in 1979 and 1980 by investigators in NYC and Boston. (Peterson 1979, Holzworth 1980) The question at that time and since then has been: Is hyperthyroidism a new disease in cats? Based on epidemiologic and hospital-acquired data, the answer appears to be “yes”. During a 14 year period from 1970-1984, an average of 1.9 cats per year were diagnosed with hyperthyroidism; however, it is now estimated that the incidence is as high as 2% of the feline population seen in tertiary care veterinary facilities. (Peterson 1994, Edinboro 2004) Since then, hyperthyroidism has become the most frequently diagnosed endocrinopathy in the cat with reports stemming from North America, Europe (esp UK), New Zealand and Australia. Hyperthyroidism in cats has become increasingly more prevalent due to an increase in the number of cats that survive past 10 years of age, because of improved diagnostics and because of increased suspicion for the disease among veterinarians in practice. Dozens of studies have been published on the origins of feline hyperthyroidism; however, none provide a definitive answer to the mystery behind this disease.

Nutritional aspects of hyperthyroidism

Canned cat food has been implicated as a cause of feline hyperthyroidism in multiple epidemiological studies. (Kass 1999, Martin 2000, Edinboro 2004) The suspected goitrogen is bisphenol-A-diglycidyl ether (BADGE), a substance used in making the liner of easy-open “pop-top” cans. It is suspected that this compound can leach into the foods and be consumed by cats. While this BADGE-based lining is generally considered safe and is used for foods for human consumption, cats may be more susceptible to toxic effects of this compound because they have a greatly reduced ability to detoxify it via hepatic glucuronidation. Bisphenol A also reduces triiodothyronine binding and causes increased TSH secretion resulting in hyperthyroidism and goiter in rats and some humans. While cat studies may not be available, rodent studies show a very high safety margin. (Poole 2004) It should be noted that epidemiological studies showing associations are not the same as cause and effect. Over 90% of cats in the US consume commercial pet foods as their primary nutritional source, and relatively few develop hyperthyroidism.

Molecular aspects of hyperthyroidism

More recently, investigators have honed in on the molecular aspects of feline hyperthyroidism. The disease in cats is more similar to toxic nodular goiter in humans and is characterized by autonomous growth of thyroid follicles. The pathogenesis of toxic nodular goiter is an abnormality in the signal transduction of the thyroid cell. The
TSH receptor on the thyroid cells activated receptor-coupled guanosine triphosphate-binding proteins (G proteins). Uniquely, the thyroid cell proliferation and hormone production are both controlled by the TSH receptor-G-protein-cAMP signaling. Overexpression of stimulatory G proteins and underexpression of inhibitory G proteins have been demonstrated in some humans with toxic nodular goiter. (Derwalht 1995, Delmer 1992) Mutations of the TSH receptor that result in the receptor remaining activated without ligand (ie, TSH) have also been reported in humans with toxic nodular goiter. (Parma 1997, Fuhrer 1997, Holzapfel 1997, Russo 1996)

In hyperthyroid cats, the same abnormalities have been investigated and it appears that activation mutation of the TSH receptor may be part of the pathogenesis of feline hyperthyroidism in some cats. (Peeters 2002) Furthermore, abnormalities of G proteins, specifically significantly decreased G inhibitory protein expression, has been described in tissues from hyperthyroid cats. (Hammer 2000)

Environmental aspects of hyperthyroidism

In one study, the use of cat litter was associated with an increased risk of hyperthyroidism (Kass 1999); however, there was no significant difference between different litter brands suggesting that the use of litter is simply a marker of cats that are kept indoors. (Peterson and Ward 2007) Indoor cats are likely to live longer and hence have a higher risk of developing hyperthyroidism. Exposure to pesticides and herbicides has been associated with thyroid abnormalities in other species. (Gaitan 1990) In particular, the use of flea control products was associated with an increased risk of developing hyperthyroidism; however, no specific product or ingredient could be identified. (Scarlett 1988, Olkzak 2005)

One recent report implicated brominated flame retardants (BFRs) as carcinogens/goitrogens possibly associated with feline hyperthyroidism. (Dye 2007) Coincidently BFRs were introduced 30 years ago at the same time that feline hyperthyroidism emerged. Bromide, a halide, is an intriguing agent to implicate in feline hyperthyroidism because of the unique composition of thyroid hormones which contain the halide iodide. In this recent abstract, serum levels of lipid adjusted serum polybrominated diphenyl ethers (PBDE) levels were 10-400-fold higher than those found in human exposure. The authors theorized that these findings of high PBDE serum levels is in accord with the most consistently identified risk factor which is “indoor living”. The authors also propose that cats are at increased risk because of meticulous grooming behavior and increased exposure to furniture and carpets. The small size of cats is also a possible risk factor for increased serum levels of PBDEs.

References

17. Peeters ME, Timmermans-Sprang EP, Mol JA. Feline thyroid adenomas are in part associated with mutations in the G (s alpha) gene and not with polymorphisms found in the thyrotropin receptor. Thyroid 2002; 12:571-5.