Feline hyperthyroidism – part one: prevalence and risk factors

ANDREW L BODEY
BVSc, CertVR, MRCVS

in the first of a two-part article, looks at the widespread occurrence of this disorder in cats, its possible causes, and elements that may impact on its development

FELINE hyperthyroidism is recognised as the most commonly identified endocrinopathy in older cats, with the first reported case as recent as 1977 (Peterson et al, 1979, cited in Peterson, 2012).

Without associated clinical signs, the first reported feline goitre was described in 1964 (Lucke, 1964, cited in Peterson, 2012) at postmortem examination. However, among 7,000 postmortems performed at the Animal Medical Center, US between 1970 and 1984, on average only 1.9 cats per year had a goitre observed prior to 1977, suggesting this disease was either novel, or at least very rare, at this time (Peterson et al, 1994, cited in Peterson, 2012).

Epidemiological surveys have reported a steadily rising prevalence to date. The most recent survey, in Ireland, reached a peak of 21 per cent of 508 cats 10 years of age or older, diagnosed by total thyroxine (T_4), irrespective of suspected thyroid status.

Although the condition is well known and diagnosis is generally straightforward, subclinical cases are estimated to be an additional 10 per cent (Sparkes, 2012; Gallagher and Mooney, 2013). Confounding factors such as increasing cat population, longer life expectancy and more frequent seeking of veterinary advice are probably insufficient to explain this change in prevalence (Mooney, 2002).

Geographic distribution is worldwide, although not uniform, with some countries such as Hong Kong, Italy and Romania under-represented. There is no sex bias, but purebreds such as Siamese cats (**Figure 1**) and Himalayans are under-represented, whereas domestic short and longhaireds are the most frequently affected (Feldman and Nelson, 2004).

Causes

Approximately 95 per cent of feline hyperthyroidism cases are caused by functional thyroid adenomas, varying in diameter from 1mm to 30mm (Figure 2), 70 per cent to 75 per cent of which are bilateral and up to 20 per cent of which are ectopic (intrathoracic). Cysts are not uncommon (**Figures 2** and **3**).

Carcinomas account for less than five per cent of reported cases, although this prevalence has been shown to increase to 20 per cent after a period of four years on medical management with methimazole (Peterson and Broome, 2012, cited in Peterson, 2012).

This observation has led Peterson to suggest although a causative link to methimazole is possible, it is perhaps more likely both adenomas and carcinomas share a common pathogenesis and it is the passage of time in these patients that allows progression of tumour type.

Risk factors

Epidemiological surveys have suggested a number of risk factors (**Panel 1**), although association does not prove causation. Perhaps chief among these is the assertion "the feeding of commercially prepared cat foods is one leading candidate as a major risk factor for development of thyroid pathology and hyperthyroidism in cats" (Peterson, 2012). With the exception of the most recent epidemiological survey (Gallagher and Mooney, 2013), all others have identified an increasing proportion of canned cat food as a risk factor, and in a UK survey, cats eating canned cat food were three times more likely to develop hyperthyroidism (Wakeling et al, 2009). In support of his controversial statement, Peterson cites several referenced factors.

Polyphenolic isoflavones are found in soy ➪

ABSTRACT

Feline hyperthyroidism is the most commonly encountered endocrinopathy in older cats. First described in 1979, the most recent epidemiological survey identified a prevalence of 21 per cent. The underlying pathological change is functional adenoma (97 per cent) or carcinoma (three per cent) and, although the aetiology of tumourigenesis remains incompletely understood, it is suggested to be the same for both tumour types. The incidence of carcinoma has been observed to increase to 20 per cent after prolonged methimazole use, suggesting prolonged exposure to risk factors allows disease progression. From this incomplete understanding, a number of preventive measures can be suggested. Although of unproven benefit, these provide a starting point for informed discussion with the most committed clients, perhaps motivated by prior or current experience of feline hyperthyroidism in a multi-cat household.

Keywords: feline hyperthyroidism, aetiology, prevention, prevalence

IMAGE: The Hyperthyroid Cat Centre, 2014.

Figure 1. Siamese cats are under-represented, but hyperthyroidism should still be a differential diagnosis. This individual had typical clinical signs of weight loss and polyphagia, and a total thyroxine of 138.4nmol/L. **Figure 2.** Goitre (right-sided in this example) can be substantial and is usually well circumscribed.

Mr Chivers from Manchester, euthyroid after RIT

⇨ continued

protein – a cheaper protein source identified in 60 per cent to 75 per cent of commercial cat foods, and are well-recognised goitrogens in rats. They have the capacity to interfere with thyroid peroxidase (the same mechanism as methimazole) and deiodinase, although have little impact when animals are also fed iodine-supplemented food.

However, in conjunction with a relatively iodine-deficient diet, T_4 and tri-iodothyronine (T_3) are substantially reduced. This results in elevated thyroid-stimulating hormone (TSH), thyroid hyperplasia and development of autonomous adenomas and carcinomas, as postulated by Peterson (Figure 4).

It is suggested a similar process may be relevant in cats, and one feeding trial with soy protein has confirmed a modest disruption to T_4/T_3 homeostasis in cats. Perhaps paradoxically, subnormal TSH in euthyroid cats has been associated with subsequent development of hyperthyroidism, although this association was interpreted not as causation, but subclinical hyperthyroidism (Wakeling et al, 2011).

The role of dietary iodine in the development of hyperthyroidism is not known. Dietary iodine concentrations have varied substantially since the first case of feline hyperthyroidism was recorded. It is known the concentration of iodine in commercial food can show 30-fold variations between different foods. In the 1980s, commercial diets contained up to 10 times recommended levels, whereas in the 1990s the level of dietary iodine was below detection in up to 25 per cent of commercial foods.

Cats fed commercial diets with relatively low iodine concentrations have shown a four-fold increase in the incidence of hyperthyroidism, compared with controls fed recommended dietary iodine concentrations (Peterson, 2012). Peterson suggests wide swings in dietary iodine may contribute to the development of thyroid disease, and that it is possible some cats may be fed on iodine-deficient diets, predisposing them to thyroid hyperplasia and hyperthyroidism.

A number of thyroid-disrupting chemicals have been suggested as risk factors. Bisphenol A (BPA) shares a similar molecular structure to T_4 and T_3 (Table 1) and Peterson suggests its well-documented effects in man and experimental animals, which include thyroid dysfunction, may be achieved by interfering with TSH signalling through TSH receptor antagonism, with consequent elevations in TSH and goitrogenic effects, as described earlier.

BPA is widely used as an epoxy resin to line cans and hard plastic bottles, to improve product lifespan (of both food and container) and is ubiquitous in food, drink, air, dust and soil. Small cat food tins are less likely to include BPA. Peterson suggests the TSH receptor interference of BPA may offer some explanation, as BPA can leach especially into fatty food during the heating process.

BPA is also present in plastics including cling film and plastic feeding bowls. BPA in rats is cleared via glucuronidation and it is known this route is under-developed in cats, perhaps allowing higher levels to be reached than in other species.

Similarly, flame retardants are well known to interfere with thyroid physiology and major production started in 1979, just before the start of the current epidemic. They are bio-accumulating organic pollutants found in packaging and in significant concentrations in house dust. Like BPA, these comprise two six-carbon rings and are known to disrupt levels of T_4 and T_3 in experimental animals.

Blood concentrations in cats reach 20 to 100 times those observed in man and it is suggested house dust – via ingestion from grooming – is the main route for exposure to cats. The route of detoxification is uncertain in cats and this may, in turn, explain the much higher levels seen in them. A direct correlation between flame retardant concentration and hyperthyroidism has not yet been demonstrated. However, Peterson regards there to be compelling evidence of a potential role, with competitive antagonism with TSH a potential mechanism.

The potential role of the cat as a sentinel species for man, as a result of this bio-accumulation, has been suggested, since hyperthyroid cats have three-fold the flame retardant concentration of younger non-hyperthyroid cats, and toddlers have 10-fold the concentration of their parents (Dye et al, 2007).

Other risk factors associated with hyperthyroidism include herbicides, pesticides (including veterinary-prescribed topical and environmental flea control) and cat litter. Cat litter may be associated indirectly, in that cat litter use may indicate cats kept mostly – or entirely – indoors, for which life expectancy is greater. This, in turn, would allow longer exposure to higher levels of environmental thyroid disruptors.

Indoor cats have significantly higher levels of – for example – flame retardants, compared with feral cats, indicating the domestic home is more contaminated than the wider environment. Also, perhaps cats kept mainly indoors would have a higher proportion of commercially prepared cat food in their diet.

In man, a genetic basis for hyperthyroidism has been suggested by the identification of mutations in the TSH receptor gene, and studies have shown similar mutations in the adenomatous nodules of hyperthyroid cats (Watson et al, 2005).

Conclusion

The aetiology of feline hyperthyroidism remains complex and incompletely understood. It is most likely multifactoral, with genetic, nutritional and toxic components, compounded by the lifestyle of the cat, grooming behaviour and limited detoxification pathways.

Against this background of incomplete understanding, Peterson suggests a collection of strategies intended to reduce the incidence of hyperthyroidism, although without any proven impact. They are summarised in Table 2 and are perhaps best suited to the most committed client, motivated by prior or current experience of hyperthyroidism within a multi-cat household.

Panel 1. Potential risk factors associated with the development of feline hyperthyroidism

- Polyphenolic isoflavones, a goitrogenic component of soy protein (a cheaper protein source), identified in 60 per cent to 70 per cent of commercial cat foods.
- Excess or deficiency of iodine in food.
- Deficiency of micronutrients in food.
- Bisphenol A, a thyroid-disrupting constituent of can and bottle liners, and plastics.
- Flame retardants such as polybrominated diphenyl ethers.
- Herbicides.
- Pesticides, including flea control used both on the cat (as a spot-on) and in the environment.
- Cat litter.

Based on Peterson, 2012.

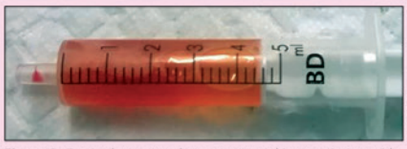


IMAGE: The Hyperthyroid Cat Centre, 2014.

Figure 3. Cystic change can be encountered in association with thyroid tumours; aspiration of the goitre in **Figure 2** yielded straw-coloured content.

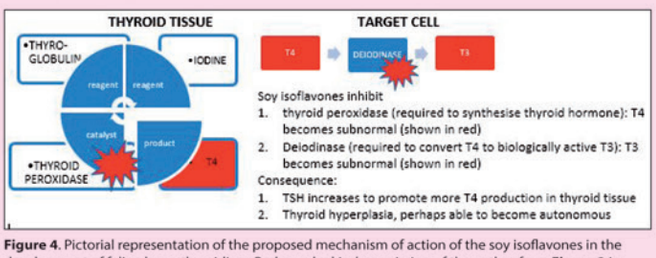


Figure 4. Pictorial representation of the proposed mechanism of action of the soy isoflavones in the development of feline hyperthyroidism. Redrawn by kind permission of the author from **Figure 3** in Peterson, 2012.

Panel 2. Feline hyperthyroidism: suggested prevention strategies

Diet
- Avoid feeding soy protein (present in many cat foods).
- Minimise the feeding of fish.
- Avoid feeding food with giblet flavours.
- If feeding moist food, use pouches.
- If the preference is for canned food rather than pouches, avoid using larger cat food cans such as 156g. Instead, plan to use smaller ones such as 85g.
- Avoid extremes of iodine concentration in food and wide fluctuations in iodine concentrations between different diets. The recommended concentration is 0.5 parts per million (ppm) to 2ppm.
- Ensure the diet has a recommended balance of vitamins and minerals – especially vitamins A and D, and selenium.
- Consider home cooking to avoid potential contaminants, but see a veterinary nutritionist.
- Avoid using plastic containers for feeding, storage or heating. Avoid using cling film over food. Instead use ceramic or glass containers.

Drinking water
- Consider using a quality filter on tap water to exclude contaminants.
- Avoid bottled or de-mineralised water.

Cat litter
- If using cat litter, choose natural biodegradable types.
- Avoid cat litter that contains chemicals such as deodorisers.

Packaging
- Be aware that fire retardants can become accessible to cats – for example, when foam packing or mattresses become aged and the covering is damaged. Try to minimise this exposure.
- Avoid products, where possible, that make use of bromine-based fire retardants.

Environment
- Damp-dust the cat's coat daily.
- Bathe the cat monthly.
- Minimise house dust by vacuum cleaning frequently with an integrated high-efficiency particulate air (HEPA) filter.
- Use a HEPA air filter in your home.
- Use topical and environmental flea products sparingly.
- Minimise use of environmental chemicals in the home.

Based on Peterson, 2012

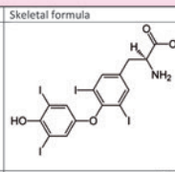
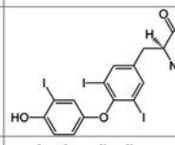
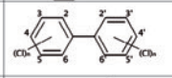
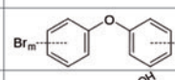
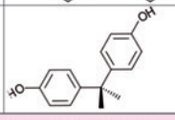
Compound	Skeletal formula	Source
T4		Thyroid peroxidase conjugates thyroglobulin and iodine within thyroid tissue (whether normal, hyperplastic, adenomatous, or carcinomatous)
T3		Converted from T4 by deiodinase enzyme within target cells, becoming biologically active and regulating cell metabolism
Polychlorinated biphenyls		Now banned in some countries, these are bioaccummulating organopollutants
Polybrominated diphenyl ethers		Flame retardants, widely used since major production started in 1979
Bisphenol A		Epoxy resin used to line tins, bottles and plastics, ubiquitous distribution

Table 1. All compounds comprise two six-carbon rings, with polychlorinated biphenyls and polybrominated diphenyl ethers having halogens other than iodine. These are known thyroid disruptors. Bisphenol A (BPA) has no halogens and has different side chains from thyroxine and tri-iodothyronine. It is proposed that BPA is a competitive antagonist of thyroid hormone receptors, causing an elevation in thyroid-stimulating hormone.

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ANDREW BODEY qualified from the University of Bristol in 1989 and in 2008 established the first radioiodine unit in the north of England. Building on this experience, he co-founded the Hyperthyroid Cat Centre near Wetherby in 2013, reducing the minimum hospitalisation period to seven days. He is also a participant in the clinical research outreach programme run by Mark Holmes at the University of Cambridge.