

## The Evolution of Feline Hyperthyroidism

The prevalence of hyperthyroidism in cats has increased dramatically since first reported in 1979.

Cats are living longer now, mostly due to better home and veterinary care. More attentive medical care includes more diagnostic testing. Therefore, hyperthyroidism is more likely to be diagnosed in cats that live long enough to develop the disease.

Even so, these factors are unlikely to solely account for the rapid increase in cases. In fact, multiple factors (genetic, dietary and environmental) seem to influence thyroid disruption and hyperplasia.

By identifying risk factors as well as goitrogens in cats' environments, we might learn ways to prevent feline hyperthyroidism, and safeguard cats' human companions as well.

This newsletter summarizes current evidence for the causes of thyroid disease in cats, and measures that can be taken to help prevent it.

### History

Just before the first cases of feline hyperthyroidism (HT4) were reported in the late 1970's, polybrominated diphenyl ether (PBDE) -flame retardants were introduced into household materials, including furniture cushions, mattresses, carpet padding and electronics.

**12-Second Flame Rule:** In 1975, Technical Bulletin 117 (TB117) was introduced in California. It required the filling, usually polyurethane foam, inside furniture and carpet pads, to withstand an open flame for 12 seconds. This standard dramatically increased the use of flame retardant chemicals in furniture and baby products across North America. "Children's products, including car seats, changing pads and nursing pillows also fall under TB117. A 2011 study showed that about 80 % of baby products made with foam contain flame retardants", according to Stephanie M. Lee's San Francisco Chronicle article titled "The Danger in Your Décor" (2013). Arlene Blum, PhD biophysical chemist and Founder of the Green Science Policy Institute, said, "*Even though TB117 was a California regulation, manufacturers often sold TB117-compliant products across the U.S. and Canada to avoid maintaining a double inventory and for defense against liability claims.*" Not only are the retardants harmful to our health, they do not prevent ignition, which begins in the covers rather than

the cushions, nor do they reduce flame spread, as reported in the publication, Fire Safety Science.

In 2007, Janice Dye, DVM, PhD, at the Environmental Protection Agency, presented a 23-cat study linking thyroid disease to chronic PBDE exposure. PBDE levels in the 11 hyperthyroid cats in the study were three times as high as those in non-hyperthyroid cats and up to 100 times higher than the levels in the people with whom they lived. Not only did this study demonstrate the association between PBDE's and thyroid disease, it opened the door for investigation of other potentially endocrine-disrupting compounds.

### How Do Feline Thyroid Tumors Form? Pathogenesis 101

#### Thyroid Disruption

Long term exposure to environmental thyroid-disruptor chemicals or goitrogens in food leads to thyroid goiters, probably in cats that are genetically inclined. Various disruptors may act synergistically or have an additive effect upon the thyroid gland

Disruption usually results in decreased thyroid hormone concentrations ( T3 and T4).

Low T4 and T3 cause loss of negative feedback, which leads to thyroid-stimulating hormone (TSH) secretion by the pituitary gland.

Increased TSH causes thyroid hyperplasia, and in turn, hyperplastic adenomas (97 %). Every HT4 cat has at least one thyroid tumor (nodule), and about 80% of the time, each thyroid gland has an adenoma. The nodules grow, become more aggressive, and, rarely, mutate into adenocarcinomas ( $\leq 3\%$ ).

The adenomas eventually develop autonomous (out-of-control) T4 and T3 production, which results in clinical hyperthyroidism. Thyroid adenomas in cats are more like 'toxic' multi-nodular goiter (MNG) in humans than Graves' disease, an autoimmune disorder affecting all of the thyroid cells.

**Epidemiological studies** identify both intrinsic (genetic) and external (exposure) risk factors and groups affected, and yield insights about disease mechanisms. Further investigation is required to prove which factors are actually correlated with thyroid disease, and if so, how much.

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## Genetics (Intrinsic Risk Factors)

At FHTC we have observed that hyperthyroidism occurs more commonly in certain families of cats. We've treated as many as 6 cats from the same litter in households with other unrelated, unaffected cats. This led us to advise testing even normal-appearing cats for HT4 that are genetically related to those with unequivocal thyroid disease.

*"Now scientists have been able to look for genomic DNA sequence differences between normal and hyperplastic thyroid tissue, and use next-generation sequencing technology (NGS) to determine expression", geneticist Lucy Davison, (VetMB, PhD, DECVIM, Cambridge, England) explained at ACVIM 2016. She adds, "Work is already underway to try to dissect the genetic basis of many human and veterinary endocrine diseases with the hope that such work may reveal new pathways and therapeutic and preventative opportunities". Simply put, geneticists are pursuing proof that our clinical impression has merit.*

### *Breed, Coat Color, and Hair Length As Risk Factors*

Epidemiological studies have found that certain pure breeds, i.e., Siamese, Burmese, and Himalayan (color-pointed) cats are relatively protected from the development of hyperthyroidism. It has been proposed that a potential mechanism for protection could be that cats of these breeds utilize less tyrosine in making melanin for their coats, so more is available for the manufacture of thyroid hormones. *"Color point breeds have a temperature-sensitive mutation in tyrosinase, which limits ability to convert tyrosine to melanin. Tyrosine is essential for both melanin and thyroid hormone production and this breed protective effect may be linked to increased tyrosine availability for thyroid hormone production."* per VJ Crossley (DVM, PhD, RVC, London).

More recently Crossley, et al, published their findings revealing British shorthairs, and Abyssinians were also at reduced risk, and that longhaired, non-purebred, domestic cats are more likely to develop HT4. Females are a little more inclined toward HT than males.

Conversely, a deficiency in tyrosine could result in thyroid hyperplasia, which could progress into autonomous hyper-productive thyroid tissue as well. There is evidence that these amino-acids are lacking in some cat foods, resulting in a lightening of cats' coats. Black hyperthyroid cats may appear 'rusty'.

Clinical expression of genetic coding may depend upon exposure to substances in cats' homes that disrupt endocrine function. This may explain why cats didn't develop clinical hyperthyroidism until the late 1970's; i.e., some may have been genetically 'primed' for thyroid disease, but fewer 'triggers' existed. Some of these disruptors are chemicals in the (home)

environment, and some may be in the cat's food, water and even litter.

## Disruptors (External Risk Factors)

The most likely external risk factors fall into two main categories, diet and environment.

### Diet:

Ingrid van Hoek ( DVM, PhD Aimargues, France) evaluated the 9 retrospective studies that investigate food-associated risk factors for HT4, and saw " insufficient evidence to conclude canned diet is a food-associated factor in etiology of HT". Even though each individual study was inconclusive, dietary factors remain suspect. For instance, Dr. Hoek explains, " bisphenol A (BPA), polybrominated diphenyl ethers (PBDEs), isoflavones, selenium, and iodine contents are suggested to cause a decreased serum thyroid hormone concentration and stimulate secretion of thyroid-stimulating hormone (TSH), leading to thyroid overstimulation and hypertrophy of follicular cells."

Even though PBDEs and BPA may cause thyroid disease, it's not clear that commercial cat foods contain enough of either to tip the scales.

**Iodine deficiency:** Iodine is essential for thyroid hormone production. In parts of the world deficient in iodine, goiters are endemic in humans. Iodine deficiency results in an increase in TSH, which gradually causes autonomous nodules (goiters), which increase thyroid hormone synthesis when even a small increase in iodine intake occurs. A retrospective study showed that cats fed commercial diets without iodine supplementation were 4 times more likely to develop HT compared to cats eating I<sub>o</sub>-supplemented cat foods. (Edinboro CH, et al. Thyroid, 2004)

Conversely, iodine excesses can also result in increased T4 production.

The upper safe limit for I<sub>o</sub> in commercial cat foods hasn't been defined by the National Research Council, although the European Union has established a maximum. The NRC-recommended minimum is 88 µg per cat per day.

**Soy:** Isoflavones from soy can act as alternative substrates for iodination. One study showed that diets high in soy can cause high T4 and free T4 levels, but the isoflavone concentration in the soy-containing diets was much higher than that in commercial cat foods.

**Dynamic Duo:** Diets that are simultaneously high in soy and iodine-deficient are much more goitrogenic than either alone (Hock).

## Environment

Licking chemical-laden dust from their coats appears to be the greatest source of goitrogens in cats. They spend a lot of time on furniture and floors where the dust forms. Humans

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may inhale the dust or in the case of children, play on floors and transfer dust hand to mouth. Hence cats may be the ideal sentinels to assess PBDE and PFC exposure in children.

Although goitrogens are also in food packaging and biomagnify in the food chain, these are lesser sources, and may not be enough alone to cause disease.

## Chemical Culprits

**Polybrominated diphenyl ethers (PBDE's)** are added to carpet pads, furniture cushions, and electronics as flame-retardants and are a major constituent of house dust. Like BPA, PBDE has structural similarity to thyroid hormones. Janice Dye's research showed that PBDE levels are significantly higher in the serum of hyperthyroid cats than healthy cats. Cats have been shown to have up to 100-fold higher concentrations of PBDEs in their serum than do humans.

**Bisphenol A (BPA)** is a plasticizer used in epoxy-coatings in food cans. It leaches into foods consumed by cats. Like PBDE, BPA has structural similarity to thyroid hormones and might act as a thyroid hormone receptor antagonist. It causes reduced triiodothyronine binding and increased TSH secretion, which causes goiter in rats, humans and quite possibly cats. Cats may be more susceptible to toxic effects than humans because they have a reduced ability to detoxify it via hepatic glucuronidation. Even so, the amount of BPA that ends up in cat food from the can lining is barely detectable (well below European Union maximum allowable), and epidemiological association doesn't prove cause and effect.

**Perfluorinated Compounds (PFCs)** are used as non-stick coatings in cookware and are applied to carpets, upholstery, mattresses, and clothing to make them more stain and water-resistant, e.g. Scotchgard®)

Both PBDEs and PFCs are highly stable in the environment, resisting chemical and photolytic degradation. They also biomagnify in the food chain and bioaccumulate in tissues. PFC's have very long half-lives (4-8 years) in humans. More studies are needed to assess how the higher serum levels in indoor cats and increasingly in humans, are associated with disease syndromes.

**Prevention:** Identifying and reducing exposure to endocrine disruptors in living spaces and diets may be key to preventing thyroid disease in cats. Reducing chemicals in our homes through regulation is the mission of the Green Science Policy Institute, founded by Dr. Arlene Blum in 2006.

## Green Science Policy Institute

According to Dr. Blum, *"Every day, the U.S. produces or imports 42 billion pounds of chemicals", many of which lack adequate regulation. Levels of toxic chemicals are increasing in humans, animals, and the environment. Compared to previous generations, our children have much higher rates*

*of health problems connected to chemical exposures."* These include, but aren't limited to: allergies, ADHD, birth defects, cancer, and diabetes.

The Green Science Policy Institute is comprised of scientists (environmental and civil engineers, chemists, physicians, etc.) with a mission to *"bring together industry, government, academics, non-governmental organizations (NGO's) and citizens to strategize technical and policy solutions to reduce the use of toxic chemicals."* They've compiled hundreds of peer-reviewed scientific studies showing the harm flame-retardants cause to humans, animals and the environment.

## TB117-2013: the New Standard:

Due in large part to the work of GSP, a replacement standard, TB117-2013 took effect in 2015. It can be met without flame retardant chemicals, though it does not restrict the use of flame retardants. Products made after 2014 should contain fewer chemicals and have labels indicating whether or not chemicals are used.

*"Recent efforts in California to eliminate flame-retardant usage in household materials has resulted in lower PBDE serum levels in Californian cats"* (Guo W, et al. Temporal changes in PBDE levels in California house cats and a link to cat hyperthyroidism. Environ Sci Technol).

## What We Can Do To Prevent Feline Hyperthyroidism:

### Diet

*It may be best to avoid:*

- **SOY**
- **BPA** in canned food linings
- **Fish** can biomagnify chemicals such as PBDE's, PFCs, and BPA and may be high in iodine.
- **Plastic** food and water bowls and storage containers (replace with glass, ceramic or metal)
- **Ultra-high** (fish, kelp) **or ultra low iodine diets** (Hill's y/d®), especially in combination with soy or other goitrogens.

### Environmental hazards

*Reduce exposure to:*

- **Stain-guard applications** in fabrics and non-stick coatings (perfluorinated compounds)
- **Furniture with foam cushions, and mattresses that have flame-retardants and stain-guard compounds.** ASK when purchasing products with cushions and read tags. Select chemical-free furniture from companies,

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## INSIDE - The Evolution of Feline Hyperthyroidism

such as Ikea®, that manufacture furniture that satisfy new TB117-2013. Products made before 2015, and are “California TB117 compliant” generally include chemicals. Those manufactured after 1/1/2015 are more likely to be chemical-free and have tags stating, “meets flammability requirements of California TB117-2013 with no chemicals”.

One option for older, chemical-probable, furniture is to replace the foam and keep the piece.

Dispose of old foam cushions, mattresses and electronics at hazardous waste stations so they can be disposed of properly to keep PBDEs from polluting the environment.

- **Carpets and rug pads** that have been treated with flame-retardants and stain-guards. Get rid of old carpets and install tile or wood flooring, or buy ‘green’ (chemical-free) carpeting and pads.
- **Newly treated floors** that are still off-gassing
- **VOC’s** (volatile organic compounds) fumes from cookware with non-stick coatings (e.g., Teflon®) and paints. Buy “VOC-free”
- **Electronics:** As of 2011, WA State Department of Ecology enforces a ban prohibiting PBDE’s in televisions and computers as well as upholstered furniture.
- **Dust:** vacuum regularly with high-efficiency (HEPA) filters and dust with damp cloths.

- **Air ducts:** clean them and change filters regularly
- **Ventilation:** especially in shower, laundry and cooking areas
- **Second-hand smoke**
- **Humidity:** maintain relative humidity between 30-50% (lessens mold and bacteria)
- **Pesticides:** Pesticides and herbicides have been associated with thyroid abnormalities in other species, so it’s reasonable to assume they would negatively impact thyroid function in cats as well.
- **Clay litters** (which may contain goitrogenic additives such as silicates). Side note: clay litters take years to degrade in landfills, so aren’t environmentally friendly despite being somewhat “natural”.

There is still much work to be done in understanding the role of genes and the environment in feline endocrine disease. Reducing chemical exposure in our homes may play the greatest role in subduing the current epidemic of feline hyperthyroidism, and may improve the health of their human companions too.

For more information about ways to protect people and cats from environmental toxics, see the Green Science Policy Institute’s web site: [greensciencepolicy.org](http://greensciencepolicy.org).

We dedicate this newsletter to Dr. Arlene Blum with admiration and respect.

*We’re available for consultation any time – please contact us if you have any questions.*

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