Frequently occurring hyperthyroidism in pet cats: it is like raising the canary-in-the-coal-mine issue

... he (the veterinarian) warned, "these cats back here are radioactive." He meant that literally. The previous day, all five animals received carefully titrated doses of radioactive iodine, designed to destroy the overactive cells that had proliferated in their thyroid glands and flooded their bodies with hormones. These cats are among the millions suffering from hyperthyroidism, one of the most mysterious diseases in veterinary medicine… [Anthes 2017].

Why is it that we are now facing an epidemic of thyroid disease in cats? Dr. Mark Peterson was one of the first to investigate the disorder. When he entered veterinary school in 1972, it seemed that feline hyperthyroidism didn't even exist. Today, Dr. Peterson treats almost nothing else. The disease was first described in 1979 [Peterson 1979]. Since then its prevalence has increased dramatically [McLean et al. 2014].The state of hyperthyroidism is now accepted as being the most common feline endocrine disorder and an important cause of morbidity in middle-aged cats in the United States, Canada, Europe, Australia, New Zealand and Japan.

Hyperthyroidism is a multi-systemic disorder resulting from excessive circulating concentrations of thyroxine and tri-iodothyronine. In fact, the cats suffer from an overproduction of thyroid hormones. The disease develops in middle-aged and older cats with no obvious breed or gender predilection to be found in most epidemiologic studies [Peterson 2012]. The disease affects many organ systems because of an overall increase in metabolism, weight loss, increased appetite, and poor body condition. Several studies have attempted to identify risk factors involved in the development of hyperthyroidism. The most likely candidates fall into two broad categories: (1) nutritional deficiencies as well as excesses in cat food, leading to metabolic thyroid dysfunction, and (2) the presence of thyroid-disrupting compounds in the cat's environment, drinking water, or food.

Several epidemiologic studies suggest that cats fed mainly on canned food run a higher risk of developing hyperthyroidism [Peterson 2012]. An accusing finger has been pointed to several flavour additives used in canned food, to plastic linings in easy-open (pop-top) lids, which may contain the thyroid disruptor chemical bisphenol [Edinboro et al. 2004a], and also to goitrogens such as soy isoflavones, generally present in dry cat foods [Bell et al. 2006]. Moreover, a huge variability in iodine intake over time may also contribute to the development of thyroid disease in cats [Edinboro et al. 2004b].

Like polychlorinated biphenyls in the past, polybrominated diphenyl ethers have now become ubiquitous persistent organic pollutants. Polybrominated diphenyl ethers (PBDEs) are synthetic brominated compound that are used as flame retardants in a variety of consumer products such as electronics, furniture and textiles, as well as construction materials. Over the past 30 years, PBDEs have become major global contaminants. They have been detected in human adipose tissue, serum, and breast milk samples [Birnbaum & Staskal 2004; Covaci et al. 2008; Coakley et al. 2012; Marchitti et al. 2017]. Exposure occurs predominantly through the diet and the indoor environment, more

particularly indoor dust. Even when the toxicology database is still relatively limited available results in the current literature raise concern.

Since PBDEs are known thyroid disruptors, these chemicals may play a role in the pathogenesis of thyroid tumors and hyperthyroidism in cats. Intensive PBDE production began just before hyperthyroidism was first reported in 1979. This supports the hypothesis that PBDEs might cause the disorder. In a study designed to determine whether the PBDEs body burdens of affected cats were greater than those of non-affected cats, PBDEs were analyzed in serum samples from 11 hyperthyroid and 12 euthyroid house cats. The results support the hypothesis that cats are highly exposed to PBDEs: a variety of PBDE congeners[1] was detected in all cats, with overall PBDE levels in cats being 20 to 100 times higher than median levels in US adults [Dye et al. 2007]. However, due to a fairly high variability within each group, no association was detected between hyperthyroid cats and serum PBDE levels. In a follow-up study, investigators measured PBDEs, polychlorinated biphenyls and organo-chlorinated pesticides in serum samples from 16 hyperthyroid and 10 euthyroid Californian household cats [Guo et al. 2012]. Their results indicate that both groups of cats had extremely high serum PBDE levels, with values that were roughly 50 times higher than the levels in human residents living in California. Moreover, PBDE congener patterns in these cats resembled patterns found in house dust, suggesting that house dust, rather than diet, is a very likely route of exposure to PBDEs in domestic cats [Mensching et al. 2012].

One year ago Ada lived on the streets; now she is treated like a princess in her new home

A small literature survey shows that cats appear to metabolize PBDEs differently to other species thus far studied. Very low levels and even a complete absence of hydroxylated PBDE metabolites were observed in cats. Moreover, statistical data treatments indicate an association between elevated PBDE concentrations in the cats and the occurrence of feline hyperthyroidism [Norrgran et al. 2015], and a correlation between cat serum PBDE levels and household dust PBDE levels. The

[1] In chemistry, congeners are related to each other by origin, structure, or function [Wikipedia].

latter finding confirms the hypothesis that dust is a significant exposure route for cats [Norrgran et al. 2017].

In conclusion, domestic cats can be highly exposed to PBDEs, presumably through the ingestion of household dust during their normal grooming behavior. They revel in the sunshine and roll around in the sand. They like to sleep on our beds, sofas and stuffed chairs; and they like it even better when there is a cat-sized mat, blanket or forgotten shirt or pull-over on top of the furniture. They lick their paws and fur all the time and end up ingesting anything that is present in the dust. There is also compelling evidence for the possible role of PBDEs in the development of thyroid tumors and feline hyperthyroidism.

However, the role of PBDEs is complex and complicated. Chow et al. [2015] conclude that the aetiopathogenesis[2] of feline hyperthyroidism is likely to be multifactorial and includes genetic, nutrional as well as environmental factors rather than one single aetiological agent, whereby PBDEs interact synergistically with other factors. Yet, additional investigation into the role of PBDEs in the development of hyperthyroidism in cats is certainly warranted.

By the mid-2000s, it was clear that PBDEs could alter the thyroid function in rodents, birds and fish. The United States and the European Union have now largely phased out these chemicals. Even so, they remain ubiquitously present. PBDEs take years to degrade, and many people still own products manufactured before they were taken off the market.

Sick animals can be seen as the "sentinels" that warn us of looming threats to human health. *For household chemicals, cats and dogs, which tend to spend nearly all their time in the home and happily hoover up whatever detritus falls on the floor, may be particularly useful sentinels…* [Anthes 2017]. Our pets are exposed to many of the same kinds of chemicals that we are. When you observe a health problem in your pet friends, then watch out! All the residents could possibly face the same fate. The results of the by now 10-year-old Dye et al. [2007] study supported the hypothesis that pet cats may serve as sentinels to better assess human exposure and adverse health outcomes related to low-level, but chronic PBDE exposure.

The comparative medicine approach [Rabinowitz et al. 2009 &2010], as applied to the study of laboratory animals in order to improve human health, has resulted in significant medical and scientific progress. Much of what is known about the human health risks of many toxic and infectious hazards present in the environment derives from both experimental studies in animals and epidemiological studies of exposed human populations. Yet, there is another, still highly untapped source of *in vivo* knowledge about host versus environment interactions: the investigation of diseases in naturally occurring animal populations. This approach may signal potential human health threats just as canaries warned coal miners of the risk of toxic gases [Burrell & Seibert 1914]. Animals may serve as sentinels for human environmental health hazards, due to their greater susceptibility, environmental exposure, or shorter life spans.

Rachel Carson's publication of Silent Spring [Carson 1962] helped launch the environmental movement. Her book evidenced that, like the canaries in the coal mine, dying birds were acting as

[2] The cause and development of a disease or abnormal condition [Merriam-Webster Medical Dictionary]

sentinels. Silent Spring begins with “A Fable for Tomorrow”, a true story using a composite of examples drawn from many real communities, where the use of DDT (and other biocides) had caused damage to wildlife, birds, bees, agricultural animals, domestic pets, and even humans. Carson used it as an introduction to a very complicated and controversial subject [http://www.rachelcarson.org/SilentSpring.aspx]. Through their deaths resulting from higher susceptibility, increased exposure, or recognizable signs of adverse (non-fatal) health events, the animals were warning humans of the health risks associated with a widespread use of chemical pesticides.

The “One Health” approach[3] assessing humans, pets, and their common environment will improve our understanding of chronic low-level, largely indoor, exposure to PBDEs and of the effects of exposure in both humans and animals.

And, Dear readers, I am quite sure you will understand that pets can also warn us of the health risks of many other ubiquitous contaminants. For as we are exposed to an extremely complex cocktail of contaminants, so too are our furry friends!

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