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Pets as sentinels of indoor contamination

Giulia Poma^{*}, Govindan Malarvannan, Adrian Covaci

Toxicological Center, University of Antwerp, Universiteitsplein 1, 2610 Wilrijk, Belgium

^{*}Corresponding author:

Giulia Poma: giulia.poma@uantwerpen.be

Abstract Historically, domestic and wild animals have been used as sentinels for human exposure to environmental contaminants, providing an early warning system for public health intervention. Since domestic animals, particularly cats and dogs, share their (indoor) environment with humans, they can respond to or be affected by toxic assaults like their owners. Given that, the potential for pets to act as bio-sentinels of human exposure to environmental contaminants has been explored in many scientific papers. In this chapter, an overview of literature studies of how pets have served as sentinels for human health effects resulting from exposure to several classes of environmental contaminants (such as metals, persistent organic pollutants, flame retardants, and polycyclic aromatic hydrocarbons) is reported and discussed. The possible links among the studies and/or the potential gaps in knowledge and research were also investigated. The presented studies indicated that cats and dogs are exposed to complex mixtures of industrial chemicals. The research outcomes demonstrated how pets well may be serving as sentinels for human health, as they breathe in, ingest, or absorb the same chemicals that are in our (indoor) environments.

Keywords: Pets, sentinels, human exposure, indoor contaminants, organic pollutants, metals

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1. Introduction

In the beginning of the 20th century, miners in Great Britain and the United States were encouraged to carry small animals, like canaries or mice, in the coal mines to detect dangerous concentrations of carbon monoxide in their working environment (Rabinowitz et al. 2009; Reif 2011; Sekhar and Rao-Chakra 2014). Besides being easily transportable, these animals have a high basal metabolic rate, making them exhibit symptoms of poisoning before gas concentrations became critical for the workers (Sekhar and Rao-Chakra 2014). In Minamata Bay, Japan, during the 1950s, neurobehavioral symptoms were first observed in cats that consumed methylmercury-contaminated fish, and their disturbed behavior has been called by the locals the “dancing cat disease” (Rabinowitz et al. 2005). In 1960, Rachel Carson’s renowned book *Silent Spring* implied that bird mortality related to the use of pesticides was a warning that pesticides, including DDT and other organochlorine compounds, were causing widespread toxicity in the environment that could also be a threat to human health (Carson 1962; Rabinowitz et al. 2009). More recently, the presence of reproductive abnormalities in fish, birds, amphibians, reptiles, and invertebrates has been attributed to the presence of endocrine-disrupting chemicals (EDCs) in the environment (Van Der Schalie et al. 1999; deFur 2004).

These are few examples of how domestic and wild animals have been historically used as sentinels for human exposure to toxic substances, being sensitive indicators of environmental hazards and providing an early warning system for public health intervention (Bischoff et al. 2010; Reif 2011). In particular, companion animals, e.g., cats and dogs, are considered valuable sentinels for human exposures because they are physically and physiologically similar to humans and they share their living environment with humans (Barthold et al. 2009). They are also potentially exposed to a high number of human-made chemicals, e.g. by inhaling indoor air with contaminated dust, strolling in industrial urban neighborhoods, eating factory-made pet

food added with a number of chemicals, being in contact with a wide variety of house and garden products (Backer et al. 2001; Ruiz-Suárez et al. 2016). In addition, because animals have typically shorter and physiologically compressed life-spans if compared with people, latency periods for the development of some diseases are shorter in animals (Backer et al. 2001).

Like humans, the exposure of pets to chemical contaminants would likely occur through indoor dust ingestion, dermal contact or inhalation, diet, and contact with household materials (Ali et al. 2013; Ruiz-Suárez et al. 2016). Moreover, since certain behavioral patterns of pets (e.g. living close to the ground, chewing on domestic objects, licking and self-grooming, ingesting dust) (Fig. 1.1a and 1.1b) are similar to the behavior of human toddlers, the presence of toxic chemicals in cats and dogs can also be an early warning sign for the health of children (Betts 2007; Environmental Working Group (EWG) 2008). For example, the exposure of cats to indoor dust can be comparable to toddlers, assuming similar bioavailability for chemicals accumulated in dust, so the exposure in cats is expected to reflect the toddlers' exposure (Norrgran Engdahl et al. 2017).

Since the iconic “canary in the cage” began to be used in the coal mines, the potential for all kinds of animals (pets in particular) to act as sentinels for human exposure to toxic substances has been explored in many scientific papers (Reif 2011; Ruiz-Suárez et al. 2016). In this chapter, an overview of literature studies of how household cats and dogs have served as sentinels for human health effects resulting from exposure to several classes of environmental contaminants (e.g. metals, persistent organic pollutants (POPs) and polycyclic aromatic hydrocarbons (PAHs), flame retardants (FRs)) is reported and discussed. As such, this chapter aims at finding possible links among the studies and/or to identifying potential gaps in knowledge and research.

2. Exposure of pets to indoor contaminants

The investigation of chemicals present in an indoor environment has allowed the identification of the main sources of pollutants and their bioavailability has been assessed by measuring chemical residues in tissues, organs, or fluids of animals living in appropriate habitats (López-Alonso et al. 2007). In this perspective, the use of pets as bi-sentinels of contamination makes it possible to determine the degree of environmental contamination and the extent of human chemical exposure, since they share the same environment as their owners and are exposed, at least in part, to the same pollutants (López-Alonso et al. 2007; Tomza-Marciniak et al. 2012). For example, as cats meticulously groom themselves (Fig. 1.1a), they lick off accumulated dust that can be contaminated with FRs, such as polybrominated diphenyl ethers (PBDEs); dogs eating scraps from the floor may swallow dirt and

dust tracked in from the outdoors and become contaminated with heavy metals and pesticides (Environmental Working Group (EWG) 2008; Veterinary Learning Systems 2008); dogs chewing and mouthing behaviors (Fig. 1.1b) can lead to oral exposures to a variety of chemicals (Wooten and Smith 2013). In addition, pets often ingest food packaging materials that contaminate their food resulting in cumulative exposures with unknown health risks (Environmental Working Group (EWG) 2008). Therefore, the knowledge of the contamination status in these animal populations is an important first step, not only to estimate the magnitude of indoor pollution, but also to predict human health risks from exposure to environmental contaminants (Storelli et al. 2009).

Fig. 1. A cat shows typical grooming behavior (photo of Brisbi taken by Giulia Poma) (left panel) and a dog shows chewing and mouthing behavior (photo of Pippa taken by Celine Gys) (right panel).

2.1. Pets as biosentinels of contamination with metals

In recent years, there has been an increasing ecological and global public health concern associated with environmental contamination by toxic metals, able to induce toxicity at low level of exposure (Tchounwou et al. 2012). Human exposure to toxic metals has risen dramatically because of an exponential increase of their use in several industrial, agricultural, domestic and technological applications. Reported sources of toxic metals in the environment include geogenic, industrial, agricultural, pharmaceutical, and domestic effluents (López-Alonso et al. 2007). While certain metals (e.g. copper (Cu), chromium (Cr), iron (Fe), magnesium (Mg),

zinc (Zn)) are essential nutrients requested for various biochemical and physiological functions, other metals, such as arsenic (As), cadmium (Cd), lead (Pb), and mercury (Hg), have no established biological functions and are considered as non-essential metals. Because of their high degree of toxicity, these non-essential elements are known to induce multiple organ damage even at lower levels of exposure and rank among the priority metals that are of great public health significance (Tchounwou et al. 2012).

In 2006, a study aimed at determining blood Pb concentration in dogs from two urban areas and in surrounding rural areas of India and at analyzing Pb concentrations in dogs in relation to environmental (urban/rural) and animal variables (age, sex, breed and housing) was published (Balagangatharathilagar et al. 2006). Blood samples were collected from 305 dogs of either sex from urban and unpolluted rural localities. The results clearly demonstrated that the urban dogs had significantly higher mean Pb concentration (0.25 µg/mL) than rural dogs (0.10 µg/mL) and that in stray dogs, either from urban or rural locality, the mean blood Pb level (0.27 µg/mL) was higher than that of pets (0.20 µg/mL). The locality (urban/rural) was considered as the major variable affecting blood Pb concentration in dogs. In particular, the blood Pb concentration in dogs was significantly influenced by breed and housing (pet/stray) in the case of dogs from urban areas and only by housing in dogs from rural areas. The higher Pb residues found in the blood of urban dogs was considered an indication of their exposure to excess lead from the environment, probably due to pollution of urban localities with the emission from industrial units and automobile exhausts (Balagangatharathilagar et al. 2006). In addition, the elevated environmental Pb content and possible contamination of food for dogs might have contributed for the higher blood Pb residue in the studied urban canine population.

To evaluate the utility of dogs as biosentinels of human exposure to metals, the concentrations of four toxic metals (namely As, Cd, Hg and Pb) in canine liver and kidney was investigated in Lugo (Spain) (López-Alonso et al. 2007). The authors have then compared between dogs from rural (most of the day outside, but coming indoors overnight) and urban (most of the time inside the house) habitats. The influence of diet, sex, and age on the accumulation of toxic metals was also considered. Mean As residues in the dogs were similar in the liver (12.6 ng/g wet weight, ww) and kidney (15.9 ng/g ww) and were not significantly affected by any of the variation factors considered. On the contrary, the mean Cd concentrations were significantly higher in the dog kidney (175.5 ng/g ww) than in the liver (58.0 ng/g ww), varying significantly with both age and sex, but not being influenced by diet and habitat. Mean Hg residues were significantly higher in the kidney (53.4 ng/g ww) than in the liver (32.7 ng/g ww), significantly influenced only by the habitat: Hg concentrations in kidney of dogs from urban areas were higher than in dogs from rural areas. Mean Pb concentrations were significantly higher in the liver (57.7 ng/g ww) than in the kidney (23.1 ng/g ww), affected only by the diet: dogs fed commercial diets showed higher Pb residues than dogs fed home-made or mixed commer-

cial and homemade feeds respectively. The mean concentrations of toxic metal observed in these dogs were in general below concentrations considered high for dogs (liver: 0.5–1.0 (As), 1.0–7.0 (Cd) and 3.6–5.0 (Pb) $\mu\text{g/g}$ ww; kidney 0.5–1.0 (As), 4.0–17.0 (Cd) and 5.0–10.0 (Pb) $\mu\text{g/g}$ ww) (Puls 1994). This is most likely because Lugo is a relatively unpolluted area.

In 2010, a case study involving a US farm in which Pb-containing paint was found as the major source of contamination for the animals was presented (Bischoff et al. 2010). Among the farm animals, measurable Pb concentrations were documented in the blood of a dog (0.15 $\mu\text{g/mL}$) and a cat (0.08 $\mu\text{g/mL}$), and two different sources of Pb exposure in the farm were identified: Pb paint on the barn for the cat and Pb paint on the house for the dog. The cat probably ingested Pb from the floor and barn dust that accumulated on his fur through grooming behavior, while the paint removal from the house (in undergoing renovation) was the most likely source of Pb contamination for the dog, via inhalation and ingestion of Pb paint dust (Bischoff et al. 2010).

The concentrations of Pb and Cd were investigated in serum of 48 healthy pet dogs from an urban area of northwestern Poland (Tomza-Marciniak et al. 2012). The mean concentrations of the analyzed metals were 0.49 and 0.31 $\mu\text{g/mL}$, respectively. Of all the factors analyzed, the body size had the largest effect on the concentrations of metals, while neither age nor sex had a significant effect on the metal concentrations in serum. In addition, it was hypothesized that small dogs could be more vulnerable, since they are lower to the ground and inhale larger amounts of dust, soil particles and deposited particulates, which carry toxic metals (Tomza-Marciniak et al. 2012).

Literature data concerning Hg concentrations in household pets are still scarce. In order to fill this gap, the concentrations of total mercury (HgTotal) were assessed in 26 dog blood and hair, and the use of household pets as sentinels for human environmental exposure to Hg was investigated in Portugal (Sousa et al. 2013). The obtained results, independent of gender, age and diet type, showed relatively low concentrations of HgTotal in the surveyed dogs, with values ranging from 0.16 to 12.4 ng/g in blood and from 24.2 to 826 ng/g in hair. Since inorganic Hg has a higher excretion rate in the organism than methylmercury, it is poorly accumulated and therefore the measured HgTotal concentrations tend to reflect the methylmercury concentrations (Tchounwou et al. 2012). In this study, a highly significant positive correlation was found between blood and hair Hg concentrations, validating the latter as a surrogate, non-invasive matrix for the evaluation of Hg exposure (Sousa et al. 2013).

The presented studies (Table 1.1) fully support the idea that pet animals, living in both urban and rural areas, may be indicators of environmental metal pollution, providing information about the potential exposure of humans to these toxic substances.

Table 1. Summary of reported data on metal concentrations in pet cats and dogs.

Country	Year	Metal	Species	Sample type (units)	Concentrations	Reference
India	2006	Pb	Dogs	Blood (µg/mL)	urban dogs = 0.25 ± 0.01 rural dogs = 0.10 ± 0.01 stray dogs = 0.27 ± 0.01 pets = 0.20 ± 0.01	(Balagangatharathilagar et al. 2006)
Spain	2007	As, Cd, Pb, Hg	Dogs	Liver and kidney (ng/g)	As: liver = 12.6; kidney = 15.9 Cd: liver = 58.0; kidney = 175.5 Pb: liver = 57.7; kidney = 23.1 Hg: liver = 32.7; kidney = 53.4	(López-Alonso et al. 2007)
USA	2010	Pb	Cats/Dogs	Blood (µg/mL)	cat = 0.08 dog = 0.15	(Bischoff et al. 2010)
Poland	2012	Pd, Cd	Dogs	Serum (µg/mL)	Pb = 0.49 ± 0.07 Cd = 0.31 ± 0.05	(Tomza-Marciniak et al. 2012)
Portugal	2013	Hg	Dogs	Blood and hair (ng/g)	blood = 0.16 - 12.4 hair = 24.2 - 826	(Sousa et al. 2013)

2.1. Pets as biosentinels of contamination with persistent organic pollutants and polycyclic aromatic hydrocarbons

POPs are organic compounds that, to a varying degree, resist photolytic, biological and chemical degradation, characterized by low water solubility and high lipid solubility, leading to their bioaccumulation in fatty tissues (Ritter et al. 1995). POPs include different classes of contaminants, among which organochlorines, such as polychlorinated biphenyls (PCBs), and organochlorine pesticides (OCPs) are persistent in the environment and of bioaccumulative nature (Kunisue et al. 2005). Although their production and use have been restricted or banned in most industrialized countries, considerable amounts of these compounds are still circulating in the ecosystem (Storelli et al. 2009). PAHs are ubiquitous environmental pollutants containing two or more fused benzene rings that are produced during the incomplete combustion of organic matter and during human or industrial activities (Guo et al. 2012b). Because of their efficient metabolism, PAHs are not POPs, but due to their high prevalence in the environment and their lipophilicity, PAHs are usually considered as pseudo-POPs (Lammel et al. 2013).

Exposure to these pollutants has been linked to a wide range of potent biological effects including immunosuppression, carcinogenicity, reproductive toxicity, and endocrine disruption in wildlife and humans (Ritter et al. 1995; Storelli et al. 2009). However, information on residue concentrations of POPs (and PAHs) in companion animals is still fragmented and limited (Storelli et al. 2009).

For example, the concentrations of OCPs and PCBs were determined in genital organs of pet dogs and cats and pet foods from Japan (Kunisue et al. 2005). Concentrations of POPs in dogs were relatively lower than those in cats, while residue concentrations in their diets were almost similar, implying that accumulation and elimination mechanisms of these contaminants in genital organs are different between the two species. This result suggests that pet dogs are at lower health risk by POPs, while pet cats may be at higher risk. Even if it has been reported that pet dogs may be valuable sentinels for environmental contamination by various chemicals, including POPs, this study showed that pet dogs have different accumulation patterns of OCPs and PCBs from pet cats and humans, suggesting that cats may serve as better sentinels of human exposure to environmental POP contamination rather than pet dogs (Kunisue et al. 2005).

With this background, the status of PCB and DDT contamination and the accumulation profile of individual PCB congeners was investigated in 84 pet cats and 91 dogs from Southern Italy (Storelli et al. 2009). In cats, the major component among DDTs was its metabolite p,p'-DDE, with an average value of 94.8 ng/g lipid weight (lw), while in dogs DDT and its metabolites were not detected in any animal, except

in two specimens. Also PCB concentrations were higher in cats (199.0 ng/g lw) than in dogs (41.6 ng/g lw). These findings can reflect differences of size class, dietary exposure and/or xenobiotic metabolizing systems between the species (Storelli et al. 2009). It has also been suggested that dogs might have greater metabolic capacity and elimination of POPs than cats (Kunisue et al. 2005).

The contamination levels of OCPs and PCBs were investigated in 2013 in a total of 36 pet serum samples (cats, n=20 and dogs, n=16) and 22 hair (cats, n=12 and dogs, n=10) collected from three large cities in Pakistan (Ali et al. 2013). Mean values of OCPs were higher in cat serum and hair (475 ng/g lw, 12.7 ng/g hair, respectively) than in dog serum and hair (32 ng/g lw, 10.3 ng/g hair). These results confirmed that pets may be valuable sentinels for indoor contamination by many, but not all, chemicals, and with significant differences in the target species. This might be due to differences in their diet, accumulation and elimination mechanisms, and interspecies differences.

The hypothesis of an existing relationship between environmental exposure to PCBs, OCPs via indoor environments and adverse health effects was then investigated, targeting domestic cats suffering from diabetes mellitus (DM) (Dirtu et al. 2013). Mean concentrations of OCPs and PCBs of 0.65 and 1.75 ng/mL, respectively, were measured in plasma samples collected from diabetic cats. While lower concentrations of OCPs were found in cats than in UK human serum samples (Thomas et al. 2006), the PCB profiles in cat plasma were found to mirror the general profile. Although diet was not analyzed in this study, it is often acknowledged as the main source for exposure to “legacy” POPs in humans, and it seems probable that the same source is responsible for the observed POP profile in the cat samples.

The concentrations and accumulation patterns of PCBs and their metabolites (OH-PCBs) were determined in the blood of pet cats (n=11) and dogs (n=17) collected from a veterinary hospital in Japan (Mizukawa et al. 2016). To estimate the exposure routes to these chemicals, the extent of dietary exposure of these pets to PCBs and their metabolites from representative samples of dry and wet pet food products were also determined. Median PCB concentrations in cat blood samples (48 pg/g ww) were higher than those in dog blood samples (< 7.4 pg/g ww), attributed by the authors to cat’s higher exposure levels. Interestingly, median PCB concentrations in dry pet food (120 pg/g ww for dogs and 350 pg/g ww for cats) were significantly higher than those of wet pet food (13 pg/g ww for dogs and 72 pg/g ww for cats), implying that PCBs in raw materials are concentrated during the manufacture of dry pet food products. OH-PCBs were detected in the blood samples of both species (median of 120 pg/g ww for dogs and 93 pg/g ww for cats), while only a few OH-PCB congeners, at extremely low concentrations, were found in the pet food, suggesting the biotransformation of PCBs to OH-PCBs in dogs and cats.

To explore metabolic capacity differences between dogs and cats and the hypotheses that domestic dogs might not be good sentinels for human exposure to POPs (Kunisue et al. 2005; Storelli et al. 2009; Ali et al. 2013), the role of the dog as

monitor of human exposure to PCBs, OCPs, and PAHs was investigated (Ruiz-Suárez et al. 2015, 2016). In the first study, the authors determined the concentrations of 16 PAHs, 18 PCBs and 19 OCPs in samples of typically consumed feeds for dogs and cats and calculated the daily dietary intake of these pollutants in both species (Ruiz-Suárez et al. 2015). The levels of the same pollutants were then measured in the plasma of 42 dogs and 35 cats, fed on the analyzed commercial feeds. The levels of pollutants were found higher in dog food (median Σ PAHs of 22 ng/g ww, Σ OCPs of 15 ng/g ww, Σ PCBs of 8.5 ng/g ww) than in cat food (median Σ PAHs of 7.6 ng/g ww, Σ OCPs of 6.2 ng/g ww, Σ PCBs of 2.4 ng/g ww) and the results showed that the median values of intake were about twice higher in dogs than in cats for the three groups of pollutants (Σ PAHs 275 vs 142, Σ OCPs 233 vs 83, Σ PCBs 102 vs 44 (ng/kg bw/day), respectively). As expected, considering the median intake, the plasma levels of PAHs were higher in dogs than in cats. However, despite the higher intake in dogs, the plasma levels of OCPs and PCBs were found from 2 to 23 times higher in cats than in dogs. This reveals a lower capacity of bioaccumulation of some pollutants in dogs, likely related with their higher metabolizing capabilities. Considering that exposure to POPs in vertebrates is likely through food ingestion, these results suggest that dogs seem to be able to efficiently metabolize and eliminate some POPs and that domestic cats may represent a better model to assess human exposure to these chemicals (Ruiz-Suárez et al. 2015). In the second study, the authors determined plasma concentrations of 56 POPs (27 PAHs, 11 OCPs, and 18 PCBs) in the plasma of 87 dogs and 100 people from the Canary Islands (Spain) (Ruiz-Suárez et al. 2016). The mean values of PAHs were 782 ng/g lw for dogs and 1624 ng/g lw for humans and it was hypothesized that the lower concentrations of PAHs detected in the plasma of dogs could be due to a higher rate of biotransformation and elimination thereof or to the presence of different routes and extent of exposure. Also for OCPs, the values of most of the target contaminants were much lower in dogs (75.6 ng/g lw) than in humans (mean 724 ng/g lw), and with different pollution profiles between the two species. With respect to PCBs values, the medians were almost 20 times lower in dogs than in humans (24.3 vs. 364.7 ng/g lw). It was then concluded by the authors that, in the light of the obtained results, it does not appear that pet dogs can be used as suitable indicators or sentinels for human exposure to POPs and PAHs.

Table 2. Summary of reported data on the concentrations of persistent organic pollutants and polycyclic aromatic hydrocarbons in pet cats and dogs.

Country	Year	Compound	Species	Sample type (units)	Concentrations	Reference
Japan	2005	POPs	Cats/Dogs	Genitals/ pet food (ng/g lw)	PCBs, M ^a dog = 8.8 ± 5 OCPs ^b , M dog = 10 ± 6.3 PCBs, F ^a dog = 20 ± 19 OCPs, F dog = 30 ± 29.8 PCBs, M cat = 78 ± 32 OCPs, M cat = 189 ± 180.3 PCBs, F cat = 77 ± 55 OCPs, F cat = 166 ± 172.2 PCBs, dog food = 5.4 ± 4 OCPs, dog food = 25.5 ± 32.1 PCBs, cat food = 5.9 ± 7.4 OCPs, cat food = 7.1 ± 5.9	(Kunisue et al. 2005)
Italy	2009	POPs	Cats/Dogs	Adipose tissue (ng/g lw)	PCBs dogs = 41.6 PCBs cats = 199 DDT dogs = 76.9 DDT cats = 99.8	(Storelli et al. 2009)
Pakistan	2013	POPs	Cats/Dogs	Serum, hair (ng/g lw, ng/g hair)	PCBs, dog serum = 18 ± 3.9 PCBs, cat serum = 47 ± 32 OCPs ^c , dog serum = 32 ± 23 OCPs, cat serum = 475 ± 635 PCBs, dog hair = 0.1 ± 0.15 PCBs, cat hair = 0.5 ± 0.4	(Ali et al. 2013)

					OCPs, dog hair = 10.3 ± 10.2 OCPs, cat hair = 12.7 ± 6.8	
UK	2013	POPs	Cats	Plasma (ng/mL)	PCBs = 1.75 OCPs = 0.66	(Dirtu et al. 2013)
Japan	2015	PCBs	Cats/Dogs	Blood/ pet food (pg/g ww)	Dog, blood < 7.4 ^d Dog, dry food = 120 Dog, wet food = 13 Cat, blood = 48 Cat, dry food = 350 Cat, wet food = 72	(Mizukawa et al. 2016)
Spain	2014	POPs PAHs	Cats/Dogs	Pet food (ng/g ww) Plasma (ng/g lw)	PAHs = 21.86 ^d dogs; 7.58 ^d cats OCPs = 14.84 ^d dogs; 6.24 ^d cats PCBs = 8.49 ^d dogs; 2.37 ^d cats PAHs = 423 ^d dogs; 253 ^d cats OCPs = 25.1 ^d dogs; 47.9 ^d cats PCBs = 50.8 ^d dogs; 89.2 ^d cats	(Ruiz-Suárez et al. 2015)
Spain	2015	POPs, PAHs	Dogs	Plasma (ng/g lw)	PCBs = 24.3 ± 26 OCPs ^e = 75.6 ± 52.7 PAHs = 782 ± 323.8	(Ruiz-Suárez et al. 2016)

^aM: male; F: female; ^bSum of DDT, HCH, HCB, CHL; ^cSum of HCB, DDT, HCH; ^dMedian ^eSum of DDT, HCB, HCH, Cyclodienes

2.3. Pets as biosentinels of contamination with brominated flame retardants

Brominated flame retardants (BFRs) are industrial chemicals produced to delay the spreading of fire and added to construction materials, indoor decorations, furniture, textiles, electronics, and electrical appliances (Alaee et al. 2003). Due to their extensive applications in these products, many of the BFRs are now ubiquitous environmental contaminants (Norrgran Engdahl et al. 2017). PBDEs, one of the major classes of BFRs, are of concern since they may target the endocrine system and also undergo debromination, leading to the formation of lower brominated PBDE congeners that possess higher bioavailability potencies (Hakk and Letcher 2003). Since they are not chemically bound to the product material, PBDEs can leach out of the products over time and accumulate in dust, which serves as a sink for these kinds of compounds in indoor environments. Due to their grooming behavior, pets are particularly exposed to chemicals accumulated in indoor dust, making them good markers for indoor exposure to BFRs (Norrgran et al. 2015; Norrgran Engdahl et al. 2017). To date, several international agreements on the regulation and use of some PBDEs have been introduced, opening the way for the introduction of other flame retardants (novel flame retardants – NBFRs), used as replacements to comply with fire safety regulations in commercial products (Dodson et al. 2012). However, most of these replacement compounds are also persistent and bioaccumulative, and their toxicological effects are still not well understood (Venier and Hites 2011).

In an early study, the US Environmental Working Group (EWG) investigated the extent of exposures of pets to several classes of contaminants (including PBDEs) in indoor environment and found that American pets are polluted with even higher concentrations of many of the same synthetic industrial chemicals that researchers have recently found in people (Environmental Working Group (EWG) 2008; Veterinary Learning Systems 2008). Composite blood serum samples were collected from 20 dogs and 37 cats, and analyzed for PBDE contamination. Concentrations of PBDEs were 113 ng/g lw in dogs (on average 2.7 higher than in humans) and up to 986 ng/g lw in cats (23.4 times higher than in humans). For both species, the potential sources of exposure were suggested to include foam furniture and bedding manufactured before 2005, contaminated air and house dust, and food contaminated with PBDEs (Environmental Working Group (EWG) 2008), while, especially for cats, a significant portion of PBDEs may come from dietary sources (e.g. seafood) and dust ingestion (Dye et al. 2007; Environmental Working Group (EWG) 2008).

Concentrations of PBDEs and NBFRs were determined in cat and dog serum and hair samples from Pakistan (Ali et al. 2013). Mean concentrations of PBDEs in cat and dog serum samples were 72 ng/g lw, significantly higher than those found in human serum from the same region, and 1.9 ng/g lw, respectively. In the same study,

the concentrations of PBDEs and NBFRs (including bis-2,4,6-tribromophenoxyethane (BTBPE), DBDPE, and tetrabromophthalate (TBPH)), were also detected in hair collected from the same cats (mean 5.15 and 7.2 ng/g, respectively) and dogs (mean 0.65 and 4.7 ng/g).

To explore the main exposure routes, ingestion of PBDEs from cats via house dust and via cat food was investigated in Sweden (Norrgran Engdahl et al. 2017). House dust from 17 homes and pet cat serum were collected, while cat food was purchased to match the diet reported. Paired samples of cat serum, house dust, and cat food were analyzed for PBDEs and the NBFR, decabromodiphenylethane (DBDPE). The mean concentrations of PBDEs analyzed in cat serum, house dust, and cat food were measured at 63 pmol/g lw, 1,435 pmol/g dry weight (dw), and 2.0 pmol/g lw, respectively. DBDPE was found in high concentrations in all dust (mean 386 pmol/g dw) and food samples (mean 1.4 pmol/g lw), but was below detection limit in serum samples, suggesting low or no bioavailability for DBDPE in cats. A correlation between cat serum concentrations and household dust has been established for the first time, supporting the hypothesis that dust is a significant exposure route for cats (Norrgran Engdahl et al. 2017).

The serum concentrations of PBDEs were also measured in serum of 22 pet cats and cat owners from Gran Canaria (Spain) (Luis A. Henríquez-Hernández, Elena Carretón et al. 2017). In this study, the mean PBDE concentrations were found as 5.48 and 1.62 ng/g lw in cats and humans, respectively, and the correlation of concentrations and the pattern of contamination (congener distribution and proportions) between both species was reported to be significant.

The growing use of PBDEs in consumer products over the past 30 years has paralleled the rising incidence of feline hyperthyroidism (FH), at present the most common endocrinopathy in cats (Dye et al. 2007; Nguyen et al. 2014). The risk of developing FH was associated with indoor living and consumption of canned cat food (Dye et al. 2007). Dye et al. (2007) hypothesized that increases in FH were, in part, related to increased PBDE exposure, with key routes of exposure being diet and ingestion of house dust. In their study, serum samples were collected from 23 cats and analyzed for PBDEs. Mean serum concentrations were up to 12.7 ng/mL, 20- to 100-fold greater than median concentrations in US adults, supporting the hypothesis that cats are highly exposed to PBDEs. It was concluded that, by extension, due to prolonged PBDE exposure, cats may be at increased risk for developing FH.

To evaluate the concentrations of BFRs in cats from Sweden and to determine whether body burdens of these compounds differ depending on thyroid status, 138 serum samples from Swedish cats, pooled into 21 pools in accordance with cat thyroid status and age were analyzed (Kupryianchyk et al. 2009). The highest median level of contamination was found for the BDE-209, found at 52 ng/g lw and 88 ng/g lw in hyperthyroid and non-hyperthyroid cats respectively. Yet, no association between PBDE concentrations and thyroid status of cats was revealed. However, the

PBDE concentrations in serum from Swedish cats were about 50 times higher than in the general Swedish human population.

As a follow-up to the study by Dye et al (2007), the PBDE concentrations in serum samples from 26 California household cats were measured (Guo et al. 2012a). They found extremely high PBDE concentrations (mean 4,505 ng/g lw, approximately 50 times higher than concentrations in California residents), linked, by the authors, to their presence in house dust. However, no evidence that linked concentrations of PBDEs with FH was found. This may be due to the small sample size, competing or confounding risk factors, or complicated causal mechanisms (Guo et al. 2012a).

The role of PBDEs in the occurrence of FH was investigated also by measuring the PBDE concentrations in serum from 62 client-owned (21 euthyroid, 41 hyperthyroid) and 10 feral cats, together with samples of commercial cat food and home dust (Mensching et al. 2012). Median serum PBDE concentrations in euthyroid cats (2,850 ng/g lw) were not significantly different from those of hyperthyroid cats (2,517 ng/g lw), while the median serum PBDE in feral cats (883 ng/g lw) were significantly lower than in either of the groups of client-owned cats. Of the two major PBDE sources investigated in this study, relatively small amounts of PBDEs were found in canned cat food (range 0.42 – 3.1 ng/g ww), while dust (150 – 95,000 ng/g lw) was identified as a risk factor for PBDE exposure in the hyperthyroid cat's home. However, like Dye et al. (2007), this study did not support a difference in contaminant load between euthyroid and hyperthyroid cats.

In addition to hyperthyroidism, it has been suggested that direct relationships may also exist between environmental exposure to BFRs and type 2 diabetes mellitus (T2DM) (Dirtu et al. 2013). Interestingly, cats may serve as a sentinel also in this scenario, since, apart from hyperthyroidism, cats also suffer from a type of diabetes mellitus (DM) akin to human T2DM. The PBDE contamination in domestic cat plasma suffering from DM, particularly DM induced by acromegaly and T2DM, was thus investigated in 2013 in UK (Dirtu et al. 2013). The mean total PBDE concentrations in cat plasma were 0.98 ng/mL in acromegaly induced diabetes and 1.66 ng/mL in T2DM. In agreement with the study by Dye et al. (2007), the PBDE concentrations measured in cat serum were higher than those usually reported for human samples collected in the same geographical area (Dirtu et al. 2013). These data suggest a great potential for accumulation of BFRs in cats, providing further evidence to the cat's potential role as sentinel for the assessment of low-level human exposure to chemicals via indoor environments.

As listed above, the measured PBDE concentrations in cat serum were, on average, higher than those found in humans, suggesting different mechanisms of absorption and elimination of these compounds (Dye et al. 2007; Environmental Working Group (EWG) 2008; Kupryianchyk et al. 2009; Guo et al. 2012a; Ali et al. 2013). Because the previous studies have suggested that cats tend to accumulate BFRs to a higher extent than dogs and that dogs can metabolically better degrade these pol-

lutants (Storelli et al. 2009), it was investigated if pet dogs might be better biosentinels than cats (Venier and Hites 2011). The authors hypothesized that dogs may resemble better humans in their response to BFRs and therefore are better indicators of human exposure to these contaminants. In their study, the authors collected blood samples from 18 pet dogs and dog food samples, analyzing them for PBDEs and DBDPE. The average concentrations of PBDEs in dog serum and food was 1.8 ng/g ww and 1.1 ng/g ww, respectively. Lower concentrations were found for DBDPE in the dog food samples (average of 0.030 ng/g ww, probably related to processing or packaging rather than to the raw material used to produce the dog food), but this compound was not detected in any of the dog serum samples. The concentrations of PBDEs in these dogs were not correlated with any of the animal-specific variables (i.e., age, weight, or daily time spent outdoors), except for the dog's weight, suggesting that dogs might accumulate PBDEs mainly through their diet, since daily feeding portions are based on weight, rather than age (Venier and Hites 2011). The lower concentrations of PBDEs measured in dogs compared to cats (from the above listed studies) can eventually suggest that cats biomagnify these compounds more than dogs, that dogs metabolize these compounds more rapidly than cats, or that dogs are exposed to much lower concentrations of these compounds (Venier and Hites 2011).

Finally, the potential role of pet cats as sentinels for human exposure to organophosphorus flame retardants (PFRs) was evaluated for the first time in cat serum from Gran Canaria (Canary Islands, Spain) (Luis A. Henríquez-Hernández, Elena Carretón et al. 2017). PFRs are currently considered as more environmentally friendly and safer than the BFRs and are being increasingly employed in consumer products. Although PFRs have been present in industrial formulations since 40 years ago, information about their environmental fate or their effects in humans and biota is however still scarce (Luis A. Henríquez-Hernández, Elena Carretón et al. 2017). In this study, a total of 11 compounds were measured in the serum of 22 pet cats and 20 humans. Mean of total PFRs in cats was 1,049 ng/g lw, not significantly different from the mean of total PFRs measured in humans (712 ng/g lw). Although some PFR compounds were found at higher concentrations in serum of cats than in human, in general terms both patterns of exposure were virtually overlapped, suggesting that cats may play a potential role as sentinels of the human exposure also to PFRs.

Table 3. Summary of reported data on flame retardant concentrations in pet cats and dogs.

Coun-try	Yea-r	Com-pound	Spe-cies	Sample type	Concentrations	Reference
USA	2007	PBDEs	Cats	Serum (ng/mL)	12.7 ± 3.9	(Dye et al. 2007)
USA	2008	PBDEs	Cats/dogs	Serum (ng/g lw)	cats = 986 dogs = 113	(Environmental Working Group (EWG) 2008)
Sweden	2009	PBDEs	Cats	Serum (ng/g lw)	hyperthyroid = 52 ^a non-hyperthyroid = 88 ^a	(Kupryianchyk et al. 2009)
USA	2011	PBDEs, DBDPE	Dogs	Serum/dog food (ng/g ww)	PBDEs, serum = 1.8 ± 0.4 PBDEs, dog food = 1.1 ± 0.2 DBDPE, serum < LOQ DBDPE, dog food = 0.03 ± 0.006	(Venier and Hites 2011)
USA	2012	PBDEs	Cats	Serum (ng/g lw)	4505 ± 1006	(Guo et al. 2012a)
USA	2012	PBDEs	Cats	Serum/dust (ng/g lw) cat food (ng/g ww)	euthyroid = 2,850 ^a hyperthyroid = 2,517 ^a feral cats = 883 ^a house dust 150 – 95,000 cat food = 0.42 – 3.1	(Mensching et al. 2012)
Paki-stan	2013	PBDEs, NBFRs	Cats/Dogs	Serum and hair (ng/g lw, ng/g hair)	PBDEs, cat serum = 72 ± 285 PBDEs, dog serum = 1.9 ± 1.1 PBDEs cat hair = 5.15 ± 7.3 PBDEs dog hair = 0.65 ± 0.3	(Ali et al. 2013)

3. Conclusions

The present review of scientific literature indicates that cats and dogs are exposed to complex mixtures of industrial chemicals, often at concentrations higher than those found in people. Several links between chemicals exposures and health risks for pets were identified, improving understanding of the risk related to low-level chronic exposure to indoor pollutants which may lead to a cumulative body burden, and adverse health outcome. The presented studies showed how pets unique behaviors may place them at risk for exposures and health risks from environmental pollutants in the home, food and consumer products (for both people and pets). These studies demonstrate that the use of pets as sentinels for indoor contamination can eventually improve the integration of human and ecological research on persistent environmental contaminants.

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