

Review

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Posted Date: 30 June 2023

doi: 10.20944/preprints202306.2104.v1

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Review

Pets, Genuine Tools in Detecting Environmental Pollutants. Sentinels and Biomonitorers

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Simple Summary: "Guardians of health," our canine and feline companions, emit early warning signals of dangerous lead, cadmium, and arsenic environmental pollution. Many of the epigenetic studies in recent years investigate the role of these pollutants in the pathogenesis of human diseases by using animal models, and analyze diseases with similar symptoms in pets and people. Not only several cancers (of bladder, mammary glands, testes and ovaries, lymphomas, mesotheliomas, carcinomas) but also hyperthyroidism, pulmonary structural changes, fertility problems, cardiac and metabolic diseases (like obesity), are at least partly triggered by environmental factors to which we are exposed. Currently, canine and feline hair can give information on the pollution or contamination degree, as well as other established biomarkers, especially regarding heavy metal and passive smoking exposure.

Abstract: In this world that we share with companion animals, they became unintended sentinels for the consequences of pollutant exposure, developing similar conditions to humans, and even earlier. This review focuses on the human-pet interaction and on the effects of the environment pets share with us. Alongside other species, canine and feline companions are veritable models in human medical research. The latency period for showing chronic exposure effects to pollutants is just a few years in them, compared to considerably more, decades in humans. Comparing the serum values of man's best friends to ours can indicate the degree of poisonous lead-load we are exposed to, for example, and of other substances as well. We can find 2.4 times higher perfluorochemicals from stain- and grease-proof coatings in canine companions, 23 times higher values for PBDEs in cats, and five times more mercury compared to the average levels obtained in humans. All these represent early warning signals. Taking into account all these, and the animal welfare orientation of today's society, finding non-invasive methods to detect the degree of environmental pollution in our animals becomes paramount, alongside the need to raise awareness on the risks carried by certain chemicals we knowingly use.

Keywords: pets; sentinels; humans; disease; environmental pollution; indoor pollution

1. Introduction

Evidence that living beings can be real sentinels of biological risks, environmental pollutants have been recognized for centuries [1]. In their book, Natterson-Horowitz and Bowers [2] point out that "In a world where no creature is truly isolated and disease spreads as fast as airplanes can fly, we are all canaries, and the entire planet it's our coal mine". Many birds, fish, wild and domesticated terrestrial mammals, and pets are valuable indicators of environmental pollution displaying early warnings of exposure to a contaminated environment before humans are affected [3].

Sentinels are organisms whose characteristics change as a result of acute or chronic effects that may be evaluated through serial surveillance. Samples may be collected routinely, at random or predetermined intervals, and analyzed to identify potential health hazards to humans and other animals [4]. There are many criteria according to which a species should be considered as a sentinel. For starters, the sentinels must occupy a large area geographically close to human settlements and humans; and their biology, have the same sensitivity to pollutants, and bioaccumulation capacity, have to be known [5]. They must be at least the same sensitive to poisoning as humans, with similar physiology, their life span must be long enough to show especially the chronic exposures, and the biological or clinical effects must develop early and be comparable to those in humans. The pathway of exposure is expected to be similar to that of humans, and companion animals share the same environment as their owners [4]. Among the phenotypic characteristics, size is essential because sufficient amounts of tissue are needed for analysis, but other aspects, such as age or gender, must also be considered [6].

With the help of pets, we can detect and intervene early to minimize the pollutants' adverse effects on human health [7]. Thus, the companion animals can literally be considered "sentinels" of environmental pollution [8].

In this paper, we aim to: 1) update information on pollutants and contaminants that affect the health status of humans and pets sharing the same environment or microenvironment 2) accepted non-invasive, early detection methods as recognized biomarkers in the identification of pollutants and contaminants with an unfavorable character on the homeostasis of the body among pets, as a starting point in epidemiological studies carried out in parallel: humans-pets 3) epidemiological studies that highlight the sentinel role of our pets in the service of human medical research 4) awareness of how we can protect them and ourselves from harmful environmental influences and increasing responsibility in the way we use certain products on a large scale.

2. Pets as sentinels for environmental pollutants

2.1. Early warning signs of an environment polluted with asbestos fibers and heavy metals

Alongside a series of wild animals, farm animals, and snakes that are considered biomonitors for soil assessment, especially when radioactive contamination is suspected [9]; raccoons (*Procyon lotor*) for trace element contamination assessment [10]; mink (*Mustela vison*) and otter (*Lontra canadensis*) for mercury environmental monitoring [11]; pets can be considered sentinels, especially for some environmental pollutants.

Pets provide useful information about harmful environmental factors and potential risks to which humans are exposed, representing patterns that show the distribution of pollution in the area [12].

Asbestos, heavy metals, and other contaminants present in the environment: air, but also water, and food, have the potential to affect the quality of life; companion animals exhibit symptoms extremely close to human intoxication [13], as shown in Table 1.

Table 1. Common symptomatology externalized by humans - pets to heavy metal action.

Heavy metal/metalloid	Pets	Action	Authors	Human	Authors
Asbestos	Dog	Canine malignant mesothelioma	[14]	Human mesothelioma	[17]
		Pleural mesothelioma	[15]	Pleural mesothelioma	[18]
		more frequently than pericardial and peritoneal origin) - poor prognostic.	[16]	more frequently	[19]
		More common in males than females		Peak incidence occurs in the 5th and 6th decades of life.	
		Pleural effusions, appear in special on old dog		Pleural effusions	
		Symptoms: Tachypnoea and dyspnea		Cough, usually nonproductive,	
		Decrease in or loss of appetite		Dyspnea	
		Lethargy, difficulty moving, insomnia, depression,		Chest pain	
		hematuria (blood in urine), hematochezia (bloody diarrhea), vomiting, enlarged abdomen and/or scrotum,		Fatigue	
		excess fluid retention, heart failure, muffled heartbeat or breathing sounds, dehydration		loss of appetite	
As	Dog	Ulcerative dermatitis	[20]	Hyperpigmentation and keratosis	[22]
		Myocarditis	[21]		[23]
		Bladder cancer		Ischemic heart diseases	[24]
	Cats	Chronic renal failure		Renal diseases	
				Bladder cancer, skin, lungs, liver, kidney cancer	
Cd	Dog	Disrupting male reproduction	[25]	Kidney damage	
		Impair pancreatic function	[26]	Alter the reproductive sphere both from the	[28]
		Decrease the bone-formation rate	[27]	hormonal point of view	[29]
	Cats	Chronic renal failure sets in		and the male reproductive organs	[30]
				Disturbances in calcium metabolism and the onset of osteopetrosis,	
				osteomalacia	
Pb	Dog	Functional disturbances of forebrain and cortical blindness	[31]	Itai-Itai disease manifested by softening of the bones	
		Anemia		Kidney failure	
		Epileptic seizures		Affects: central,	[32]
		It affects the bones by setting bone sclerosis.		peripheral, hematopoietic nervous system.	[33]
		Myocarditis chronic		Microcytic anemia	[34]
	Cats	Renal failure		Gastrointestinal disturbances	
Hg	Cats	Neurological disturbances similar to those in Minamata disease manifested by: ataxia, weakness and loss of balance and motor incoordination	[35]	Affect the renal system with the onset of renal failure.	
			[36]	Affects nervous system with symptoms such as: uncontrollable tremors, muscle loss, slurred speech, tremors, partial blindness	[37]

Canine mesothelioma has been linked to lifestyle, diet, and asbestos exposure, but the most common cases have occurred among canine companions whose owners worked in environments with asbestos or used such flea repellents in which the talc was contaminated with asbestos [38].

Human mesothelioma and malignant dog mesothelioma are clinically and morphologically similar, as reported by Harbison and Godleski [39]. The difference lies in the shorter latency period of about 8 years for canine mesothelioma versus human mesothelioma, at which onset may occur after 20 years [38]. In 2020, Otto et al. [40] closely following the evolution of the health status of human and canine rescuers after The World Trade Center terrorist attacks in the United States, did not discover any cases of mesothelioma, which was a great relief for all those involved.

Lead (Pb), cadmium (Cd), arsenic (As), and mercury (Hg) belong to the group of heavy metals/metalloids with adverse health effects, but their latency period is shorter in pets compared to humans [41]. Because the metabolism, migration, transformations, and toxicity of heavy metals are similar in pets and humans, especially in young children, the toxic effect of several pollutants, can be detected early via pets [42].

In 2005, Park et al. [43] concluded that dogs can be considered biomonitors in environmental quality assessment for cadmium, lead, and chromium contamination, but research on larger areas with cats as subjects had the same conclusive results [Table 2].

Table 2. Average values of heavy metals found in blood and vital organs in pets.

Country	U.M	Heavy metals (mean \pm SD)					Analyze d from	No. of sample s	Specie s	Autho r
		Pb	Cd	Cr	Hg	As				
Korea	$\mu\text{g/ml}$	0.68 \pm 0.19	0.21 \pm 0.01	0.66 \pm 0.15	1.10 \pm 0.49	-	Serum	204	Dogs	[43]
Zambia	$\mu\text{g/L}$	271.6 \pm 226.9	1.5 \pm 1.6	67.2 \pm 75.4	-	5.2 \pm 4.5	Blood	120	Dogs	[44]
Italy (Campania)	mg/kg	0.321 \pm 0.198	0.093 \pm 0.079	-	0.054 \pm 0.044	-	Liver	38	Dogs	[45]
		0.293 \pm 0.231	0.259 \pm 0.238	-	0.040 \pm 0.021	-	Kidney			
Italy (Naples)	mg/K g	0.256 \pm 0.130	0.098 \pm 0.063	-	-	-	Liver	290	Dogs	[46]
		0.147 \pm 0.081	0.302 \pm 0.212	-	-	-	Kidney			
		0.268 \pm 0.107	0.101 \pm 0.054	-	-	-	Liver	88	Cats	
		0.189 \pm 0.102	0.355 \pm 0.144	-	-	-	Kidney			
Poland (northwestern)		2.829 \pm 3.490	0.105 \pm 0.067		0.0020 \pm 0.0013		Cartilage with adjacent compact bone	24	Dogs	[47]
		1.55 \pm 1.71**	0.096 \pm 0.074		0.0027 \pm 0.0022		Spongy bone			
Italy (Sardinia- South)	ng/m L	81.4 \pm 16.6	52.2 \pm 14.0	-	-	139 \pm 39	Ovaries	26	Cats	[48]
		20.4 \pm 3.6	19.7 \pm 4.0	-	-	21.7 \pm 4.2	Ovaries	21	Dogs	
Italy (Sardinia North)	ng/m L	51.1 \pm 17.9	26.4 \pm 5.5	-	-	107 \pm 61	Ovaries	14	Cats	
		12.2 \pm 5.2	12.2 \pm 1.8	-	-	21.8 \pm 3.9	Ovaries	24	Dogs	

Legend: U.M- Unit of measurement; ** higher values than in humans; * lower values than in humans

The benefits of using animal sentinels to evaluate environmental lead pollution have been recognised for more than 40 years [49].

This is extremely relevant, especially when pets live in proximity to children. Preventing exposure to lead during nervous system development is very important because of the damage this heavy metal can cause [50].

The tremendous benefit of this approach is that sentinels can provide early warning without having to analyse a child's brain, using blood samples as biomarkers [4].

As early as 1976, the comparative analysis of serum samples collected from 119 children and 94 dogs from suburban Illinois demonstrated that canine companions can be considered sentinels of lead poisoning in children [49]. The presence of lead in the blood of pets that may indicate potential exposure of humans, especially young children, to the polluted environment is also the conclusion reached by Berny et al. [51].

For possible lead contamination in children, the prediction is based on canine and feline serum values that need to exceed the threshold of 2-4 times [2] [52].

Anywise, for the results to be conclusive, variables such as: sex and age of companion animals must be taken into consideration. Lead levels in the blood are higher in females than in males, and older females have higher lead build-up, according to Toyomaki et al. [44].

Apart from blood, tissue samples from the liver, kidneys and bones can also indicate the amount of lead accumulated [47]. Findings on the sentinel quality of pet animals for lead and cadmium pollution using tissue samples are highlighted by Serpe et al. [45] and Esposito et al. [46].

In analysing the ovaries of female pets, Forte et al [48] observed an accumulation of heavy metals, indicating disturbance of reproductive function.

Nowadays, according to ethical considerations, the method of sampling animals for contaminants should be non-invasive and unobstructed [53]. In this context, Petrov et al. [54], Nikolovski and Atanaskova [55] believe that using hair as a biological marker brings significant advantages in terms of ease of collection and ethical approval compared to other methods that require sampling from different tissues [Table 3].

Table 3. Mean values of heavy metals obtained from pet hair samples.

Country	U.M	Heavy metals (mean ±SD)					A.M.	No. of samples	Species	Author
		Pb	Cd	Cr	Hg	As				
Macedonia μg/kg										
Veles		930.15±516.03	54.28±12.77	-	-	-	AAS	11	Dog	[54]
Bitola		715.66±293.80	42.65±25.41	-	-	-		22	Dog	
Prilep		525.63±253.91	27.82±8.31	-	-	-		11	Dog	
Macedonia μg/kg										
Delcevo		579±478.29	68.57±59.95	-	-	-	AAS	18	Dog	[55]
Probitip		1061.38±564.02	26.86±23.30	-	-	-		20	Dog	
Veles		1099.02±593.01	171.54±179.53	-	-	-		17	Dog	
Prilep		370.57±288.39	21.65±10.64	-	-	-		18	Dog	
Bitola		687.05±482.82	66.04±73.78	-	-	-		21	Dog	
Australia	mg kg ⁻¹	1.19±3.11	-	0.85 ± 1.42	0.13±0.11	0.08±0.06	AAS	36	Dog	[56]
DW										
Argentina	mg gDW ⁻¹	-	-	-	-	24 ± 2	TXRF technique	-	Dog	[57]
Portugal	μg g ⁻¹					24±2.4	TXRF	50	Dog	[58]
Portugal	ng g ⁻¹	-	-	-		24.16 - 826.30	TXRF technique	26	Dog	[59]
Poland	mg · kg ⁻¹	-	-	-		0.025±0.020	AAS	85	Cat	[60]
Iran	ng/g DW	-	-	-			AAS	40	Wild cats	[61]
North-west		-	-	-		735±456				
North		-	-	-		568±381				
						692± 577				

Center	-	-	-	1303±1306			
				376±162			
North-east	-	-	-	1517±1888			
West	-	-	-	231±89			
Japan	ppm	-	-	7.40 ±2.93	AAS	12	Male cat [62]
		-	-	7.45±1.28		29	Femele cat
		-	-	0.99 ± 0.23		16	Male dog
		-	-	0.66 ±0.10		18	Femele dog
Alaska	ng/g			1822.4±1747		-	Sled dog [63]
Legend: U.M- Unit of measurement; DW- dry weight, AAS-atomic absorption spectrometry, A.M.- Analysis method, TXRF -Total Reflection X-ray Fluorescence Analysis							

Jafari [56] using canine hair observed a strong positive linear correlation between the contamination of the soil and their hair with chromium, copper, lead, and mercury, and to a lesser extent with zinc, and a negative correlation with arsenic.

The same promising results were obtained from feline hair as a biologic marker equally good for monitoring the environmental quality of lead. The authors' clarification consists in the fact that a larger accumulation is observed in female cats, but also with more time spent outdoors [64].

2.2. Pets and early warning signs for heavy metals in water and food

In terms of arsenic accumulation, many regions of Argentina are recognized as chronic regional endemic hydroarsenic zones due to arsenic contamination of water. A special contribution to early detection and chronic exposure to arsenic in water is canine hair, according to Vázquez et al. [57]. Arsenic values in dog hair were clearly higher than those found in water or human hair (1±1 mg gDW-1).Rodriguez Castro [58] also demonstrated that canine hair is a potential method for the assessment of chronic arsenic exposure.

Global anthropogenic pollution and climate changes affect even the most remote areas such as Greenland, and Alaskan villages [65] [66].

For terrestrial or marine environmental contaminants affecting dietary products which accumulate pollutants including mercury, sled dogs (*Canis lupus familiaris*) are sentinels that can provide early warning to local communities regarding the possible risks associated with the food they consume especially since, absorption, accumulation, and mercury excretion is similar to that of humans [67-69].

Again, dog hair is a surrogate but safe way to analyse the amount of mercury in the body during chronic exposures. The highly significant positive correlation between total mercury in canine blood and hair, as well as the blood-to-hair ratio (200) similar to that described in humans, reinforces the belief that man's best friend can be considered a sentinel of mercury exposure [59].

Findings that the use of canine hair is a reliable indicator of exposure of sled dogs to mercury were also highlighted by Dunlap et al. [63].

Cats suffer pathological changes from methylmercury poisoning similar to those produced in humans in the disease called Minamata disease, discovered in 1959, but whose initial results were never published [70]. The experiment, later taken up by Eto et al. [71], sprinkling the cats' food with liquid mercury led to observations related to the accumulation of the metalloid in the cerebrum, cerebellum, liver, and kidney. In both, humans and cats, mercury poisoning has the same symptoms, the incoordination known as "dancing cats of Minamata" being an early warning sign of intoxication [72].

In feline companions, mercury accumulation is influenced by age and sex. In geriatric males, the accumulation begins earlier compared to females and has slightly higher values in males [62]. In addition, it was proven that there is a strong correlation between the mercury content in the hair and

that found in the liver and kidneys. Hence, the conclusion drawn by Skibniewska and Skibniewski [60] is that feline hair can provide an indication of mercury exposure, and its concentration is correlated with existing loads in other vital organs (liver: 0.030 ± 0.031 , kidney: 0.026 ± 0.025 mg·kg⁻¹). Wild cat hair lends itself equally well to environmental biomonitoring, according to Behrooz et al. [61].

The first alarm signal about the potential danger that threatens the integrity of human health is the accumulation of mercury values 5 times higher in the body of pets compared to that in the human body [73].

3. Enemies hidden in the microclimate of houses

3.1. *Secondhand smoke, danger early detected by companion animals*

Human-animal interaction in terms of common lifestyle dictates many aspects of our and our pets in contact with environmental factors and pollutants. Unsurprisingly, the results of many studies involving exposure to tobacco smoke, and second-hand smoking provide a correlation between that and the incidence of nasal, lung cancer, and other diseases [74]. In a much more aware way currently, the side effects of passive smoking are documented for all those living beings who share living quarters with a smoker, companion animals included [75].

By second-hand smoke, companion animals are exposed to cotinine, heavy metals, and at least 40 compounds with genotoxic and carcinogenic potential that cause DNA alteration in the oropharyngeal tissue [43]. Due to these effects, companion animals are considered sentinels for the early destruction of DNA [76].

Cats that live in a smoke-polluted environment for more than 5 years are prone to asthma, lung cancer, lymphoma [77] or oral squamous cell carcinoma [78].

Investigations carried out between 1993 and 2000 in cats demonstrated that the risk rate of malignant lymphoma increases with their exposure to passive smoking, which constitutes alarm signals for the increase in the risk of non-Hodgkin's lymphoma among smokers [79]. A year later, Denson [80] observes that the risk of malignant lymphoma is higher in lower socio-economic groups, smokers, who cannot vaccinate cats against infection by feline leukemia virus (FeLV), and notes a close correlation between the two diseases [81].

On the other hand, starting from the hypothesis that second-hand smoke leads to an increase in nasal cancer prevalence in dogs, and taking into account factors such as the number of smokers around, the exposure period expressed in years, and the share of time spent inside the house, was found that, dolichocephalic dogs are prone to nasal cancer [82]. This aspect was also emphasized by Bertone-Johnson et al. [83].

Unlike dolichocephalic dogs, mesocephalic and brachycephalic breeds are at risk of lung cancer because they filter less tobacco smoke [84].

Consequently, cancer of the nose or lung is related to the length of the nose, an extremely important phenotypic feature [85].

The Beagle breed has been for many years a veritable model for human respiratory tract cancer. Histological changes in their lungs are similar to those observed in humans following exposure to cigarette smoke. Inhalation of passive smoke causes changes in the population of macrophages and lymphocytes, and anthracosis in the cytoplasm of macrophages with alteration of the respiratory tract [86].

In adult humans, passive smoking is associated with the risk of developing different types of cancer: breast, nasal sinuses, and nasopharynx. [87].

The study of the impact of passive smoke on the health of pets has extremely relevant connotations on the health of children. Children's exposure to passive smoking is associated with early cancer like lung [88] [89] or nasal cancer [90]. Furthermore, children can suffer from leukemia, lymphoma, liver cancer and brain tumours [91].

Human medical research to find non-invasive methods to detect exposure to tobacco smoke started with finding nicotine biomarkers from hair treatment, hair color, and growth rate on nicotine levels in hair, until hair became a reliable sampling material for epidemiological studies [92].

In order to track and quantify tobacco through inhalation, absorption, or ingestion, cotinine, an endogenous nicotine metabolic product is used as a biomarker and can be identified in pets' blood, saliva, urine, and hair [8].

Hair from cats, the only domesticated species in the *Felidae* family, demonstrates nicotine biomarker capabilities through passive smoke exposure [93].

The similarities in the expression of human and canine follicular biomarkers provides a wide range of studies on exposure to tobacco smoke and the potential risks of human illness [94]. Nicotine in the hair of canine companions, as well as in that of humans, is considered a reliable indicator of long-term exposure to passive smoking [95].

The child-pet bond was demonstrated by Knottenbelt et al. [96] who showed that similar amounts of cotinine in canine and children's hair are an early warning sign of future health problems and that it can be used as a valuable biomarker of passive smoking. But, quantifying cotinine, a toxic metabolite of nicotine in canine hair, Benowitz, N. L. [97] found that the amount of cotinine varies not only with the exposure time but also with the sex, weight, and age of the pets. Females have a higher concentration of cotinine in their hair than males.

An alternative non-invasive method of determining cotinine is to sample and test the urine of canine companions. In this case, the urine biomarker analysis takes into consideration the breed to which the canine companions belong. The explanation lies in the lower breathing rate of the heavy breeds in comparison with the small breeds [98].

Prior to this study, Roza and Viegas [86] comparing urinary cotinine concentration in 2 groups of Yorkshire Terrier, one exposed to smoke and the other not, found that urinary cotinine is a genuine biomarker of passive smoke exposure.

An alternative to identifying the concentration of cotinine, particularly in brachycephalic breeds, is saliva, which is an indicator of possible disease among homeowners. Saliva comes into direct contact with the environment in which pets live and is not filtered through the renal system [99].

3.2. *Pets, sentinels and biomonitors for Persistent Organic Pollutants and Brominated Flame Retardants- "forever chemical"*

3.2.1. Brief characterization of substances from the "forever chemical" group

"Forever chemicals" are a group of persistent substances, per- and poly-fluoroalkyl substances (PFAS), which are very resistant to decomposition due to their high electronegativity and dissociation energies of carbon-fluorine bonds [100]. These substances are characterized by persistence and are difficult to be detected, especially the PFAS, the perfluorooctane sulfonate (PFOS), and the perfluorooctanoate (PFOA). All these have a considerable bioaccumulation capacity in free-living organisms and humans. They include over 4000 compounds used in plenty of products including non-stick cookware, stain-resistant fabrics, fast food packaging, and other chemical materials. Once partially broken down, these persist in an omnipresent way in dust, water, and food, they pass through the placenta from mother to fetus, and then through milk ingestion [101].

Since the 1970s Polybrominated Diphenyl Ethers (PBDEs) have been used in numerous household products such as electronic goods, synthetic textiles, polyurethane foam, or thermoplastics, commercial materials in the form of tetrabrominated BDE-47, pentabrominated BDE-99 and -100, and hexabrominated BDE- 153, 154, octabrominated, brominated congener 209, bisphenol A (BPA) [102]. The chemical structure is similar to that of the thyroid hormones 3,3',5-triiodothyronine (T3), and 3,3',5,5'-tetraiodothyronine (T4) alters their homeostasis [103].

Using chemical additives to prevent combustion and delay fire spread after ignition (flame retardants) in the environment represents another health risk for our pets [104]. Polybrominated diphenyl ethers (PBDEs) make parts from Brominated flame retardants (BFRs) found in plastics, textiles, electronic castings, and circuitry [105].

Polychlorinated biphenyls (PCBs) comprise 209 compounds. They are a group of compounds with markedly high persistence in the environment (between 94 days and 2700 years, depending on the molecules) and high accumulation capacity in living organisms, including humans. The categories of PCBs are divided into dioxins, furans, and pesticides. Being lipophilic, PCBs tend to bioaccumulate in adipose tissue [106].

Many of the compounds are considered endocrine-disrupting chemicals (EDCs). Through similar sources and routes of exposure, environmental endocrine-disrupting chemicals (EDCs) affect the health of both humans and pets (dogs, cats) and cause multiple ailments associated with disruption of the body's homeostasis. The most frequent pathologies triggered by such dysfunctions of the endocrine system include hyperthyroidism, metabolic disorders (like obesity), reproductive problems, renal failure, and even several types of cancer [8].

3.3. Comparative human-pets epidemiological studies associated with the use of "forever chemical" substances

Parallel epidemiological studies in humans and animals indicate that exposure to a group of persistent substances is associated with immunotoxicity, cardiac and metabolic diseases, developmental and reproductive effects, cancer, and, more recently, type 2 diabetes [107] [108]. The following table [4] presents certain similarities between the human and animal bodies through the action of these compounds.

Table 4. Similarities that occur as a result of changes in the homeostasis of the human body and companion animals.

Compound	Cas	Diseases	Similar ailments	Authors
PFAS Pbdes	Cat	Hyperthyroidism	Production of endocrine and especially thyroid toxins	[109] [102]
			The presence of hyperplastic or adenomatous nodules,	[110] [111]
			Insidious onset,	[112] [113]
			Proportionally similar values of the concentration of thyroid hormones and thyroid-stimulating hormone,	[114] [115]
			Hypermetabolism manifested by progressive weight loss despite increased appetite, change in behavioral: hyperactivity, restlessness, nervousness	[116] [117]
			On cat the onset hyperthyroidism in middle or old age.	[118] [119]
Pbdes	Dog	Hypothyroidism	The histological changes of feline hyperthyroidism represent a small-scale mirror reproduction of human symptoms, moreover, the graceful companion can be a model and sentinel for individuals with toxic nodular goiter (TNG)	[120]
			Slower, lazier activity	[121] [122]
PFAS	Cat	Obesity	Weight gain without an increase in appetite	[123] [124]
			Acts as an obesogenic substance	[78] [117]
PFAS	Cat	Childhood obesity**		[125]
		Adult obesity**		
		Type 2 diabetes	Weight loss despite a good appetite	[125] [126]
		Gestational diabetes mellitus **	Polydypsia	[127] [128]
		Type 2 diabetes**	Frequent urination.	[129] [130]
			Retina and neural complications	[131]
PFAS	Dog :	Intake water	Common histopathologic features: deposition of pancreatic islet amyloid	
			Fatty tumors, Pancreatic disorders,	[132] [107]
			Various gastrointestinal disorders	[133] [134]

		Chronic liver disease ** Fatty liver disease** Hepatotoxic effect**	
PFOA, PFOS	Dog: Beagles and police dogs	Lower cholesterol	[99], [101]
		Negative association with direct bilirubin**	[135] [136]
		Changes in liver function biomarkers :βbilirubin, βalt, βalp**	[137] [138]
		Increase: Alanine Aminotransferase -ALT, <i>alkaline phosphatase</i> –ALP, aspartate aminotransferase (AST), Gamma Glutamyl Transferase -GGT **	
PFNA,PFDA		Increase circulating cholesterol concentration	[101]
		High blood cholesterol**	[136] [137]
PBDE	Dog	Poor semen quality	[42],
PCB		Testicular cancer	[139]
		Disruption of reproductive function and infertility**	[140]
		Decreased sperm counts, and genital malformations**	
Pcbs	Dogs	Liver cancer,	[114] [141]
		Meningioma	. [142]
		Pancreatic cancer ,	[143]
		Mammary cancer on female dog sentinel for breast cancer on human	[134] [144]
		Cancer: PCB concentrations > 1000 ppb (micrograms/l) and adipose PCB levels > 400 ppm (mg/kg)**	
		Other type OF CANCER: melanomas, liver, gall bladder cancer, biliary tract, gastrointestinal tract, brain**	
PCB	Cat	Lower brain weight	[111], [145]
		Decreased birth weight and head size**	
Legend: Cas- companion animals; ** human ailments			

3.4. *Pets, sentinels for "forever chemical"*

Food ingestion and dust inhalation are the primary sources of human exposure to these compounds [147]. By contrast, inhaling and ingesting indoor dust is the main route of contamination and exposure for pets and especially cats [148]. On cats, dermal exposure becomes oral exposure, as they are active groomers, being the pathway that favors the onset of feline hyperthyroidism [110].

That cats, are considered sentinels were established by the increased incidence of hyperthyroidism due to indoor dust exposure by Chang et al. [111], but also by Brake et al. [112] as a result of parallel studies on human and feline patients. They found that higher quantities of PFAS, were detected in cat serum than in humans. One of the hypotheses is that cats have different metabolic reactions to those pollutants [113].

The lifestyle of many domestic cats lacks appropriate exercise. Lack of activity leads to boredom therefore, is accompanied by excessive grooming, which provides a way to ingest PFAS that acts as an obesogenic substance. That is the conclusion of the author Bost et al. [78] looking at obesity rates in household cats.

Among canine companions, the effects of chronic exposure to PFAS, clinical manifestations such as constant hair loss, back injuries, numerous fatty tumors, pancreatic disorders, and various gastrointestinal disorders were observed by Barnes, G. [132]. Several types of PFAS have been linked to higher or lower cholesterol levels in Beagles and police dogs. [136].

Related to humans, part of the changes occurring in the homeostasis of the human body are similar to those of pets, a fact highlighted by the study conducted by Salihovic et al. [135] on 1002 human patients. The effect of PFAS exposure is positively associated with the activities of several liver enzymes, and liver function biomarkers and, inversely associated with changes in circulating bilirubin.

According to Norrgran Engdahl et al. [149], 20% of PBDE comes from the human diet or cat diet based on canned fish, but the most substantial part of the accumulation of BDE-209 congener, is caused by the presence of indoor dust.

Even though the mode of inhalation exposure of humans and cats to PBDEs compounds is similar, the level of compounds in plasma is slightly higher in cats [150]. This fact was also demonstrated in the results obtained by Dirtu et al. [151] by sampling and analyzing plasma in parallel from children between 3 and 5 years of age and their feline companions. The values obtained are very different according to the report BDE 47/99 in "favor" of cats. In their plasma, the values were similar to those found in indoor dust. In other words, these sentinels, cats, show that ingestion of dust contaminated with chemicals is a danger, especially for toothless children who come in contact with dusty surfaces more frequently and are at higher risk of ingesting dust than adults. The similar ratio between congeners B47/BDE 99 from serum sampling from cats and analysis of indoor dust provides a valuable method for identifying the cause of cat contamination. The ratio of BDE47/BDE99 < 1 with BDE 99 (predominant) indicates exposure of cats to indoor dust [152].

PBDEs present in indoor dust are also linked to an increased incidence of feline hyperthyroidism. This finding was highlighted by Mensching et al. [153] following the superimposition of feline hyperthyroidism over the exposure of cats to indoor dust through ingestion.

Evaluation of the relationship between dust ingestion and feline hypothyroidism revealed other aspects such as the serum value of Σ PBDE in cats, which is 20-100 times larger than in adult humans [154]. One of the explanations for the accumulation of higher amounts of PBDEs compounds in the serum of cats lies in the reduced activity of metabolic reactions in phase I [149].

The PBDEs compounds BDE 209, BDE 207, and BDE 47, and their derivatives can accumulate in organs and tissues such as the liver, bile, brain, and blood, depending on companion animal species. Between canines and felines, higher accumulation of BDE 209, BDE 207, and derivatives both in tissues and in the brain was found in cats, where BDE 209, BDE 207, 6OH-BDE47, 2'MeO-BDE68, and 2,4,6-tri-BPh can cross the hematoencephalic barrier [155]. In the cat liver, the congener BDE47, is metabolized much faster than BDE 99, which breaks down into OH-HBCD, which is why Zheng et al. [156] consider *Felis catus* to be a promising sentinel for human exposure to HBCD from environmental pollutants.

To observe changes in the homeostasis of the feline organism, Khidkhan [145] conducted a study in parallel by administering a single dose of a mixture of 12 PCBs and small but constant doses of over a year of BDE 209. According to results, PCBs decrease the serum albumin and total proteins, alongside the decline in testicular weight. As for BDE 209, it was correlated with decreased serum albumin concentrations, lower brain weight, and increased serum levels of high-density lipoprotein (HDL) and triglycerides, hence the conclusion of authors that chronic exposure may have adverse effects of limiting lipolysis in the liver and initiating lipogenesis from the subcutaneous adipose tissue.

In an attempt to demonstrate canine hypothyroxinemia caused by environmental pollution with PBDEs and PCBs, Lau et al. [122], found that there were no major differences in the concentration of PBDEs and PCBs in dogs diagnosed with hypothyroxinemia compared to healthy ones, only one congener, BDE 183 showing some meaning. Instead, Schilling, R.J. [123] based on the symptoms presented by people exposed to polychlorinated biphenyl (PCB) and the analysis of compounds in the plasma of canine companions, were able to demonstrate that dogs can be considered sentinels, having a greater capacity to accumulate these compounds. Moreover, the symptoms of hypothyroidism in dogs are clearly comparable to the signs of the same disease in human patients [121].

Among multiple negative effects on the body, exposure to PCBs increases the risk of various types of cancer including liver cancer, meningioma, and pancreatic cancer [141]. In support of this statement, Ferrante et al. [157] found that PCBs values resulting from the burning of plastic waste in the open air were higher in dogs diagnosed with cancer than in healthy ones.

Pets, both dogs and cats, can provide information about the decline of human reproductive function during their lifetime. Through chemical sterilization, these companions can provide information on reproductive abnormalities by analyzing the quality of the genital tract tissue and functional abnormalities reflected in quality, quantity, and viability of sperm and ovum, through routine monitoring of fertility simultaneously with the monitoring of contaminants [158].

In 2019 Sumner et al. [159] performing parallel tests on the quality and mobility of human and canine semen showed that canine companions can represent environmental pollution sentinels of exposure to diethylhexyl phthalate (DEHP) and polychlorinated biphenyl 153 (PCB153). Two years later the same authors analyzed the chemical profiles and testicular pathologies in dogs after castration from three regions of Great Britain, one location in Denmark (Copenhagen), and one in Finland (Vantaa), and through parallel investigations on human testicular cancer have demonstrated that: environmental influences and especially the presence of diethylhexyl phthalate (DEHP), polybrominated diphenyl ethers (PBDE), and polychlorinated biphenyls (PCB) have negative repercussions on male reproductive function such as the poorer semen quality and increased incidence of testicular cancer [139].

The conclusion reached by the Environmental Working Group [73] is that blood values showing 2.4 times higher accumulation of perfluorochemicals from stain- and grease-proof coatings in canine companions, 23 times higher PBDEs in cats, are early warning signals of the dangers lurking inside our home.

Chemicals found in lawn care products with carcinogenic potential were identified by Knapp et al. [160] by administering herbicides [2,4-dichlorophenoxyacetic acid (2,4-D), 4-chloro-2- methyl phenoxy propionic acid (MCP), dicamba] and then analyzing the urine from humans' best friends. The authors conclude that our companion animals can serve as sentinels for potentially harmful environmental exposures to humans. Not only urine can be considered a biomarker for the determination of pesticides, but also the feces contents in order to detect 2,4-dichlorophenoxyacetic acid (2,4-D), according to Reynolds et al. [161]. Canine feces can also be a source of useful "information" for at least 13 different PFAS compounds [100].

Acrolein used as a pesticide but also to obtain acrylic acid necessary for the manufacture of plastic, paints, adhesives, and superabsorbent polymers for diapers [162] can represent a potential health risk, especially since the values found in dogs and cats exceed the permitted thresholds [163].

Urinary biomarkers for acrolein and arsenic have a 2.8- to 6.2- fold increase in canine companions compared to owners exposed to the same mutagenic household chemicals. The preliminary tests performed by Craun et al. [164] are part of a larger project that attempts to quantify the mutagenic potential of household substances in dogs with urothelial carcinoma (UCC), which could play a sentinel role in identifying substances, the owners' exposure to carcinogens and, mutagens correlated with the occurrence of bladder cancer.

3.5. Tags, wristband, silicone collars, the new generation of methods for analyzing the compounds in the category "forever chemical"

A tool simple to implement to detect exposures to environmental contaminants, especially flame retardants, tobacco products, and PAHs, is the wearing of silicone wristbands, tags, and collars [116]. Silicone wristbands are promising passive tools to support epidemiologic studies to characterize exposure to organic contaminants, especially because the results can be obtained much faster, compared to years of latency period in many chronic diseases triggered by these pollutant agents [115]. The use of these devices reduces the time needed for sampling compared to other methods such as dust collection, and serum investigation [165]. For this reason, some testing methods have gradually been replaced by the examination of silicone collars and wristbands that can quantify the level of exposure to organic contaminants and especially to herbicides. These devices can detect with

certainly 72 existing compounds, some of them such as fipronil sulfides (degraded fipronil), and DDE' (DDT metabolites) being considered endocrine disruptors. In addition, they are cheap devices, easy to wear, non-invasive and silicone has the same potential to absorb chemicals as human or animal cell membranes [166]. More than that, between the levels of contaminants from the analysis of the tags worn by the canine companions and urinary metabolites (validated urinary biomarkers), significant correlations were obtained for several organophosphorus esters including permethrin and N,N-diethyl-meta-toluamide (DEET) [115].

In fighting fires, firefighters are exposed to numerous compounds, which raise the rate of cancer among them. The wearing of silicone tags by canine companions revealed the presence of: 18 PAH, di-n-butyl, diisobutyl phthalate, guaiacol and DEET classified as having a possible carcinogenic effect [167].

Two years later, Poutasse et al. [168] using the same devices worn by firefighters' canine companions, found that some endocrine disrupting chemicals (EDC) come mainly from household products and environments and less from areas frequented by firefighters in the fight against fire.

The consequences on animal welfare through exposure to numerous flame retardants present inside homes, predominantly BDE47 and BDE99, were highlighted by the parallel use of OPE metabolites taken from urine and silicone tags, which demonstrated once again that these tags capture information about exposure and represent valuable devices to be used in the assessment of environmental pollution in homes [109]. The wearing of silicone collars by the graceful felines and similar wristbands by owners have demonstrated that cats can be considered sentinels of human exposure to numerous contaminants, silicone collars being more sensitive to many PAH compounds [169].

Quantitative evaluation of flame retardants (FRs) that may contribute to feline hyperthyroidism was carried out using passive sampling devices made of silicone, pet tags, useful in assessing the exposure to many compounds, including the detection of Tris (1,3-dichloro-2-isopropyl) phosphates (TDCIPP). A research performed by Poutasse et al. [170] of silicone devices on 76 cats found that Tris (1,3-dichloro-2-isopropyl) phosphate (TDCIPP) associated with air freshener use has higher concentrations in hyperthyroid cats, associated with higher concentrations of free thyroxine (fT4), and total T4 (TT4).

4. Pets, sentinels and models in comparative oncological studies induced by environmental pollutants

4.1. General characterization

For a long time, pets are within the attention of researchers due to changes in homeostasis and disorders produced in the body similar to those in humans when exposed to the same environmental and pollutant factors [171].

Although there are similarities between different types of cancer and other ailments that trigger the polluted environment, pets have shorter lifespans than humans [38].

Another aspect to note is the incidence of cancer which is ten times higher in dogs, may occur spontaneously, and the latency period is shorter compared to humans, where initial signs of disease can appear after 30-35 years [172]. The analysis of spontaneous tumors in dogs is not only a broad area for exploring pathogenesis, but also greatly reduces the need for laboratory animal testing [173][174].

Despite more than 1000 strains of transgenic mice currently used in medical research [175] for environmental and genetic factors that trigger the onset of human cancer, studying the disease in dogs is more appropriate. One of the reasons is the finding that, with the canines companion we have in common over 650 million base pairs of ancestral DNA sequences, their orthologous genes share a 75% similarity with that of humans [176].

4.2. Environmental pollutants and human & pet health impacts

Based on epidemiological investigations carried out in the city of São Paulo, Kimura et al. [177] found a strong association between the spatial distribution of canine lymphoma and non-Hodgkin lymphoma. The results suggest that in the pathogenesis of lymphomas, environmental pollutants caused by vehicle emissions and heavy traffic can play an important role in the pathogenesis of this disease.

Another investigation that attests to the fact that similar human-companions animal environmental conditions are positively correlated both with neoplasm occurrence in dogs and non-Hodgkin's lymphoma in humans was carried out by Pinello et al. [178] over five years, in the Greater Porto area (north-western Portugal). The authors concluded that, in particular, male canine companions may act as sentinels to environmental pollutants associated with this type of cancer. In humans, men are more likely to have this type of lymphoma [179].

Canine lymphoma has also been, positively correlated with the habitat that pets share with their owners, with a higher occurrence near industrial areas or when owners repeatedly use certain types of paints at home [180].

Craun et al. [181] later added other risk factors. Investigating 63 boxer dogs, they highlighted the increased incidence of lymphomas near nuclear power plants, chemical product suppliers, and crematoriums.

Baioni et al. [182] comparing the cases of malignant tumors in dogs from the north-west of Italy based on the Canine Cancer Registry of Piedmont and those existing among the human population, reached the conclusion that: the records can represent a reliable reference for comparative studies in risk detection to the carcinogenic environmental contaminants to which the human community is exposed.

Another documented research, draws attention to the morbidity rates due to canine bladder cancer which according to the authors, Hayes et al. [183], may represent a sentinel condition and help in the early detection of environmental carcinogenic hazards looming over the human population living in polluted industrial areas.

Human health problems associated with persistent organic pollutants are related to immune suppression, genotoxic effects, or cancer [74]. Cumberbatch et al. [184] specify the fact that among the human population worldwide, bladder cancer ranks 9th in occurrence and 13th in annual deaths.

Several authors consider that transitional-cell carcinoma can be associated with organochlorine, organophosphorus pesticides, tobacco, and other household products [185].

The potential risk of transitional cell carcinoma of the bladder particularly in obese dogs, is related to the use of herbicides and insecticides [186]. Five years later, Glickman et al. [187] noted that treating the lawn with phenoxy herbicides leads to a considerable increase in transitional cell carcinoma (TCC) of the urinary bladder in Scottish Terriers. Bladder cancer was diagnosed following histological evidence of transitional cell carcinoma in 89 dogs exposed to insecticides used to control ticks and fleas. These acaricids and insecticides, which accumulate in fat deposits of the body, have a high potential for tumors..

As Mutsaers, A. J. et al. [188] point out, there are a number of similarities between human-dog bladder cancer related to symptoms: hematuria, dysuria, urinary tract infection most common, immunoreactivity to TAG-72 antibodies; 20% of dogs 5-10% of humans are diagnosed with metastases; the most common sites of metastasis: regional nodes and lung.

Another unfortunate consequence of human exposure to pesticides is the high risk of mammary neoplasia [189]. The exposure of pets to the same environment claims them as sentinels because of high mamary carcinoma incidences. Observations made by Andrade et al. [190] concluded that pyrethroid pesticides directly affect hormonal homeostasis, especially that of estrogens, and indirectly lead to cell proliferation or apoptosis, reducing or increasing the number of mammary epithelial cells. In 33.3% of canine females with mammary carcinoma, insecticides were found in adipose tissues.

By evaluating serum, mammary tissue, and adjacent mammary adipose tissue from female dogs patients diagnosed with mamary cancer, Gautam et al. [191] demonstrated the presence of 14

different pesticides in much higher concentrations than in samples from healthy dogs. Among them, γ -HCH was most commonly highlighted while Heptachlor, aldrin, and p, p' -DDT had a lower frequency. A positive correlation was found between the presence of tumors and the age of females. The share with the highest diagnostic rate was assessed in the four to eight years, followed by the category between eight and 12 years.

In contrast to other results in which levels of organochlorine pesticides in plasma (OCP) were higher in cats, the results of the study conducted by Yavuz et al. [192] in 15 cats and 21 dogs revealed much higher levels of OCP (α -hexachlorocyclohexane (HCH), β -HCH, γ -HCH, hexachlorobenzene (HCB), aldrin, 2,4'-dichlorodiphenyltrichloroethane (2,4'-DDT), 4,4'-DDT, 2,4'-dichlorodiphenyldichloroethylene (2,4'-DDE) and 4,4'-DDE among canine companions.

Our companion animals do their best to warn us about the potential dangers of exposure to 2,4-D, which increases the risk of malignant lymphoma in dogs associated with non-Hodgkin's lymphoma in humans and is also a danger to children's health [193].

In the cat, considered much less sociable than the dogs but a true bioenergetic device [194], the frequency of occurrence of oral squamous cell carcinoma (SCC) is relatively high. The risk of this disease may be heightened by wearing flea collars, up to five times more than in congeners without a collar [195]. There are multiple causes underlying the occurrence of oral squamous cell carcinoma in humans, including smoking, but studies undertaken by Devianto et al [196] have demonstrated that there is a more pronounced affinity among farmers exposed to sunlight and pesticides for the disease to be triggered.

Even though the results were not extremely conclusive, Enriquez et al. [197], observed that pets proposed as sentinels for some types of cancer in humans highlighted the fact that cutaneous tumors in dogs are proportional to the rate of use of pesticides or biocides by the owners.

Fipronil from the products used as external antiparasitic treatments against fleas and ticks has a residual time of about two months after administration and they can irritate the skin of pets. Consequently, cats and dogs may exhibit lethargy, incoordination, dilated pupils, facial swelling, and convulsions [198]. Human exposure to these substances results in neurotoxicity, liver and kidney damage, skin irritation, eye damage, reproductive effects, and cancer [199].

Although pets can be considered our "canaries" for a number of carcinogens, Rabinowitz et al. [71] note, canine companions have an as yet untapped potential to detect the multitude of compounds and assist in finding means of preventing human cancer.

5. One health approach. Companion animals like sentinel

When considering environmental pollution, we have to be aware that the concept is broader than just inorganic or organic compound contamination. Microorganisms (bacteria and viruses) can be considered dangerous pollutants too. In this regard, our canine companion represent biomonitors of pathogen exposure [200], since they are susceptible to various infections. People, animals, the environment and the interdependence between these three components underpin the One health approach, an emerging field [201]. At present, more than ever, zoonotic diseases have a rapid spread, and pets, especially canine companions, can be considered sentinel, early warning tool in disease prediction [202, 203].

In some cases, the dogs have multiple roles, as described in a recent paper by Balboni et al. [204] about leptospirosis. Caused by a bacterium, *Leptospira* (*Leptospira* spp.), this is a zoonotic disease with possible fatal effects in many species. Besides being susceptible to the disease, dogs can also be potential hosts and an important sentinel species for the dangerous microorganism.

Another pathogen classified as a possible biological weapon is *Coxiella burnetii*, the causative agent of Q fever, a zoonotic disease with serious debilitating potential. According to Orr et al. [205] this disease raises alarming signs among dogs in Eastern and Central Australia recently. The danger is greater among pig-hunting dogs; almost one-fifth of the tested dogs were found to be seropositive, and out of them the sterilized dogs were more susceptible than non-sterilized ones. The authors conclude that dogs can be considered sentinels of the *C. burnetii* exposure, providing early warning for humans.

Dogs can be considered sentinels for plague cause by *Yersinia pestis*. Owing to the rapid serological response to the plague bacillus among canine companions they can be deemed useful amplifiers or sentinels for the detection of plague in areas frequented by humans [206]. The research led by Rajerison M, et al. [207] demonstrated that, parallel analyzes in humans and several animal species, including dogs, showed that they have good sensitivity and performance in evaluating the SIgT test, for the detection of total Ig (IgT) anti-F1, being considered sentinels.

Dogs can also provide useful information on the risk of human exposure to *Bartonella spp.*, which is why Henn et al. [208] mentions that they can serve as sentinel system for surveillance of endemic areas.

For human and horse meningoencephalitis, produced by West Nile virus that affects many areas around the world: African continent, also in the USA (New York city), dogs can represent the reliable and alternative sentries in West Nile virus surveillance by analyzing IgG against WNV by using an in-house ELISA with inactivated WNV as antigen [209]. Komar et al. [210] noted that young animals are more susceptible, and Kile et al. [211] states that seropositivity is higher among outdoor family dogs than for indoor family dogs. Along with dogs, cats especially stray cats can serve as sentries in West Nile virus surveillance [212].

The risk of getting sick with *Trichinella spiralis* (trichinosis-zoonosis), especially among the population who eat game meat, can be avoided by taking blood from hunting dogs and, quick and cheap anti-*Trichinella* IgG detection. The method could also be implemented to identify antibodies that cause risk-related diseases of human health such as: ehrlichiosis, leishmaniasis [213], tularemia, Rocky Mountain spotted fever [214].

5.1. Enigmas of the human-animal interaction

Another enigmatic facet of the human-pet relationship is the ability of companion animals to perceive and signal certain health problems in humans. We already know about the developed sense of some dogs to detect early forms of cancer. Cancer cells in affected humans can produce and release odor signatures, volatile organic compounds that dogs can smell out from skin, breath, urine, and sweat, and can alert humans about their presence [215, 216]. With the necessary training are considered medical detection dogs because they can warn about early-stage melanoma or colorectal, lung, ovarian, prostate, and breast cancers [217,218].

In many circumstances, canines are considered helpers, protectors, and service providers. Seizure-alert dogs are trained to warn even before a person has a seizure, one of the most common neurological disorders in the world [219, 220].

They can naturally detect the change in the smell emitted by the human before the onset of a seizure or even intervene to avoid it [221, 222].

A less-known benefit of cohabitation with companion animals is that they support people's health by exposing them to animal-specific microorganisms. For example, the modern treatment for human asthma, atopic dermatitis, rhinitis, certain cardiovascular diseases, obesity, and even depression, proposes the microbiome-based approach, based on exposure to mixed microbes through the symbiosis created between humans and their pets [223]

6. Conclusions

Our canine and feline companions can act as sentinels for a tremendous number of pollutants and contaminants which have similar negative effects on their soundness than on the health of humans, especially children.

Investigating and approaching in parallel the occurrence of certain diseases of humans and pets which have a high incidence in given geographic areas can expand the field of medical research and can aid in finding more affordable solutions both in terms of sampling time and data processing.

The collaboration between human and veterinary medical laboratories represents an advantage in preventing the increase of diseases caused by environmental contaminants. Based on the results of such collaboration, the environmental and other public authorities can be warned, solutions can be

found, or activities can be implemented in order to improve the quality of the environment in which we all live.

Despite their widespread use, the possible health hazards posed by several substances and products are not known by the general public. Understanding the ways in which, many times unknowingly, we pollute our environment and understanding that we share its harmful consequences with our pets could lead to more responsible environment-protective behavior by both the pet owners and those not owning companion animals. With all the climate change, diseases that in the past did not occupy certain areas, become present. For some zoonotic diseases, pets can become real tools, true sentinel in surveillance of areas.

We, the authors, consider that general awareness has to be raised in this matter, and we hope to contribute with a grain of knowledge to this task, through our paper.

7. Future Directions

In the light of the scientific research reviewed in this paper, the benefits of centralized actions became clear. Parallel analyses in humans and companion animals to monitor national and international level mortality and morbidity linked to the degree of environmental pollution, authority level interdisciplinary collaborations in finding strategies to reduce the negative impact of polluted environments and to prevent further contamination are highly desirable. Although these actions need decisions of legal entities, we all can contribute, in our own quality: as a scientist team, a single researcher, or a simple citizen, regardless. In our consumer society the conscious and informed choice to use the available products and to care for the ways we use these can and do matter—for our pet, for our child, for our self.

Author Contributions: All authors have contributed to research and writing of the manuscript. The final version was read and agreed by all authors.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Conflicts of Interest: The authors declare no conflict of interest.

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