The Role of Companion Animals as
Sentinels
for Predicting Environmental Exposure Effects
on Aging and Cancer Susceptibility in Humans

The National Academies of
SCIENCES · ENGINEERING · MEDICINE

A Hybrid Workshop

Indoor Products:

Endocrine Disruptors, Flame Retardants, PFAS

Jan Dye, DVM, MS, PhD, DACVIM
Center for Public Health & Environmental Assessments
U.S. Environmental Protection Agency

Day 2
12-2-2021

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Disclaimer:

- The opinions presented here are those of the presenter alone and not the opinions or policy of the US EPA.

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Questions

- Why use Animals as sentinels?
  - advantages
  - shorter prepatent period
- Why use Companion Animals?
  - advantages
  - location, location, location
- Why focus on the indoor environment?
  - common exposure routes

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One Planet

90+ % Indoors

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Why cats?

- Scientists decode most of cat's DNA
- They get more than 200 diseases that resemble human illnesses …
- The list includes a cat's version of:
- SARS, AIDS, diabetes, retinal disease and spina bifida
- Feline asthma, bronchitis, idiopathic pulmonary fibrosis
- Feline hyperthyroidism, diabetes

This Abyssinian cat from Missouri, *Cinnamon*, had made scientific history.

Genome Research, Nov. 2007

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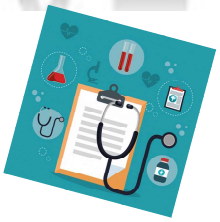
Can we …

- Lifespan

- Health data



- To use Companion Animals as Sentinels for Humans ?

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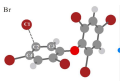
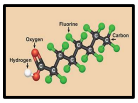
POPs & Pets: A Tale of Two Kitties

PBDEs 

Skinny (hyperthyroid) cats

https://www.vetco.org/51-content/kcik-eksperta-endokrynologia/314--top-10-signs-of-hyperthyroidism-in-cats

PFAS 

Fat cats (obesogens)

https://www.cbc.ca/news/canada/edmonton/fat-cats-feline-obesity-1.5364613

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Feline Hyperthyroidism (FH)

- Signs
  - Weight loss
- Risk Factors
  - Age > 8 years
  - Canned cat food (flavors)
  - Living indoors

ANIMAL MODELS OF DISEASE: Feline hyperthyroidism: an animal model for toxic nodular goiter

Peterson ME, Journal of Endocrinology 2014

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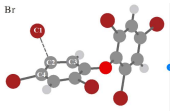
Reasons to implicate PBDEs



- Structural similarity to thyroid hormones
  - Displace T_4 from serum transport proteins
- Timing of first reports: 1979
  - (a) FH cases
  - (b) environmental contamination
- Geographic "hot spots"
  - California, Great Lakes
  - California - proactive, safety
  - PBDE levels in sludge/soil, fish, wildlife
- Cats like fish / seafood
- PBDEs routinely incorporated into household products

https://www.heartsofpets.com/cats-caught-stealing/2/

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Indoor sources of exposure

chicagotribune.com/consumer-reviews

https://www.pikist.com/free-photo-swffj

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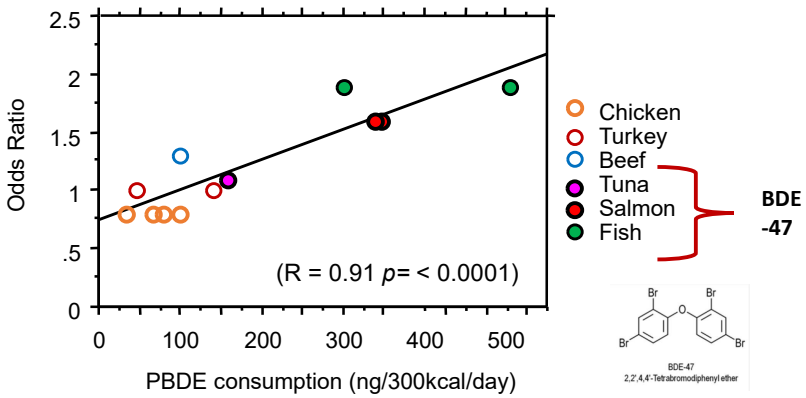
Diet Factor

Correlation of daily PBDE consumption (ng BDE/300 Kcal/day) for canned cat food vs. overall OR for developing feline hyperthyroidism



(Martin *et al* 2000).

(Dye *et al ES&T* 2007).

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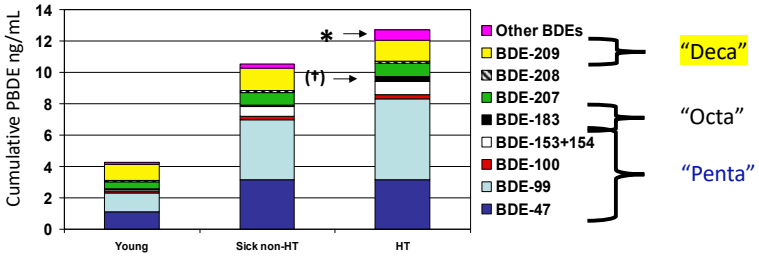
Body burdens: PBDEs in cat serum



*Significantly different than young cats (p = 0.04).

†Trend only in significant difference from young cats (p = 0.06).

- Indicative of age – or disease-dependent changes in PBDE metabolism
  - BDE-47/99 ratios were inversely correlated with age.
  - 47/99 and 100/99 ratios in HT cats were significantly lower than those in other cats.

Some cats within each group had 5X higher ∑ PBDE serum levels; "outliers".

Dye *et al ES&T* 2007

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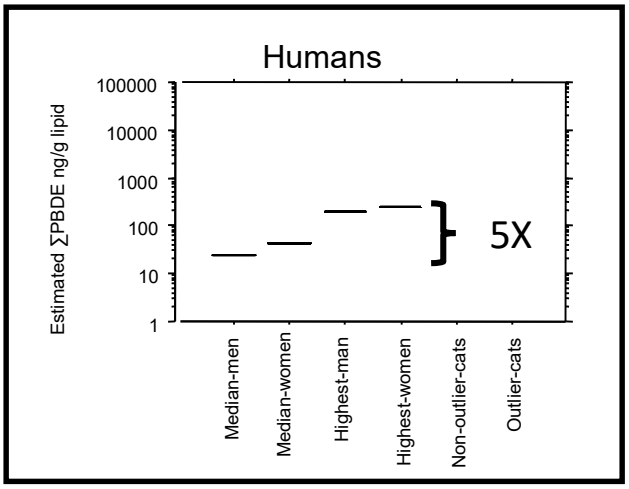
Body burdens: ∑ PBDE serum levels in U.S. humans



Schecter *et al* 2005

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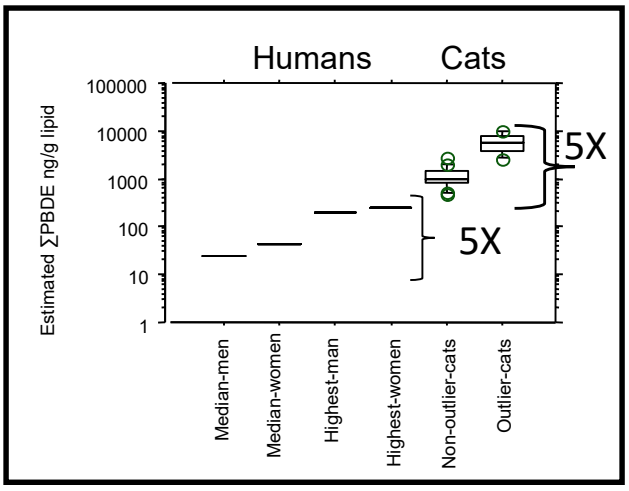
Body burdens: ∑ PBDE levels in U.S. cats and humans



Cats had 20 - to 100-fold greater serum levels than the median levels in U.S. adults.

Schecter *et al* 2005 Dye *et al* 2007

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Why are cats so highly exposed?

- Indoor cats – direct contact with PBDE-containing household materials
- PBDEs can leach/volatilize from products
- House dust - high levels of PBDEs
- Some of the most contaminated house dust: *"penta"* mixture
- Outlier cats:
  - *"penta"* mixture
- Dust ingestion via grooming

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Kids and Cats

- Young children and Indoor Cats, may be at greater risk for exposure to indoor agents because they:
  - *Inhale, contact* AND
  - *ingest* greater quantities of microbe-ladened house dust
- Children
  - increased floor contact time
  - "mouthing" behaviors
- Cats
  - increased floor contact
  - extensive grooming

https://www.epa.gov/healthresearch/understanding-exposures-childrens-environments

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Cats as sentinels for … toddlers?

https://www.epa.gov/children/childrens-environmental-health-research

- Dust ingestion estimates
  - 0.7 mg/kg/day adult
  - 1.4 -14 mg/kg/day 2-yr-old

U.S. EPA. *Exposure Factors Handbook, Vol. 1 — General Factors;* U.S. Government Printing Office: Washington DC, 1997; EPA/600P-95/002.

5 mg/kg/day cats

(Dye *et al* 2007)

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PBDEs and skinny cats

- Potential links to thyroid disease in cats
- Pet cats highly exposed
- Possibly via exposure to dust which is laden with PBDEs

(Dye *et al* 2007).

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Transdisciplinary approach

Elevated PBDE Levels in Pet Cats: Sentinels for Humans?

Janice A. Dye, Marta Venier, Lingyan Zhu, Cynthia R. Ward, Ronald A. Hites, and Linda S. Birnbaum

View Author Information

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https://doi.org/10.1021/es0708159

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Lingyan Zhu



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Transdisciplinary approach

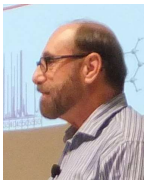
ELSEVIER

Environmental Research
Volume 151, November 2016, Pages 145-153

U.S. domestic cats as sentinels for perfluoroalkyl substances: Possible linkages with housing, obesity, and disease

Phillip C. Bost [a], Mark J. Strynar [b, 1], Jessica L. Reiner [c], Jerry A. Zweigenbaum [d], Patricia L. Secoura [e], Andrew B. Lindstrom [b, 1], Janice A. Dye [f]

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Cats as Sentinels

- Goal:
  - understand primary routes of PFAS exposure
  - Assess potential health impacts of exposure
- Cross-sectional study
- Cats: Feral, outdoor, indoor cats
- Range of ages
- Healthy and diseased subjects

- Any associations noted in a cross-sectional study design should in ***no way*** be considered causal.
- A hypothesis-generating effort by which to guide future, more focused, research.

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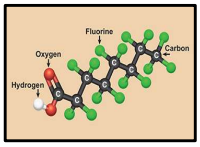
PFAS in Products



PFAS are commonly found in every American household, and in products as diverse as:

In-home usages

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Sources of exposure

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Pets and kids – common exposures

Pets and kids can be messy

Contact with treated upholstery

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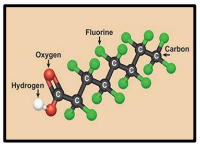
Stain Prevention Products

- PFAS: Chemical properties of the fluorocarbon tail
- Unique – is both hydrophobic & lipophobic
- "Repel" both aqueous- and lipid-based compounds (ideal surfactant)
- Function: Stain repellants



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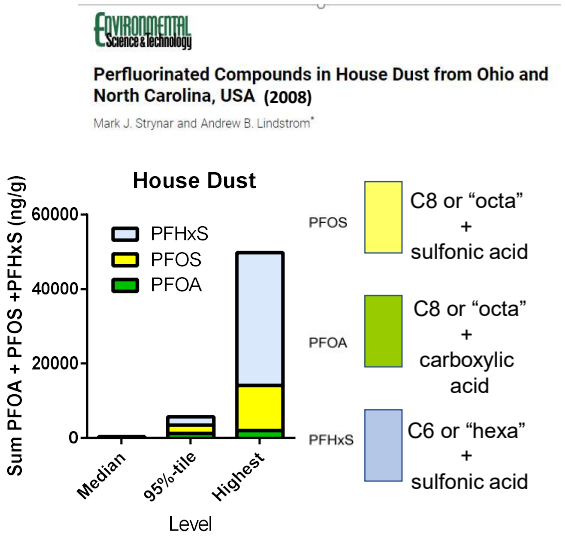
PFAS levels in House Dust



THE DUST!

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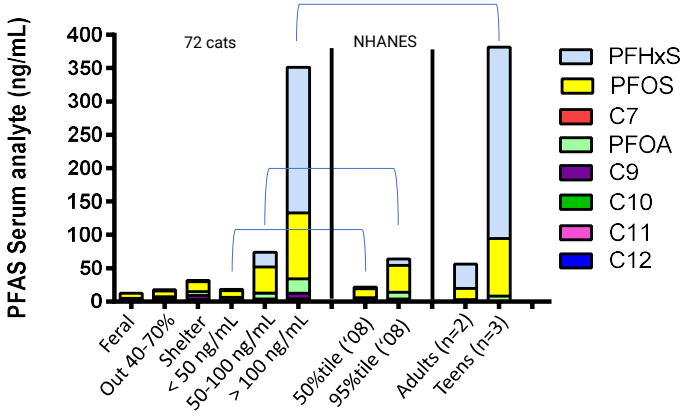
Body burdens: Serum PFAS levels in U.S. cats and humans



(Bost *et al* Env Res).

National Health and Nutrition Examination Survey - CDC

Analyte profile was consistent with the known content of a carpet anti-stain product (Beeson *et al ES&T* 2008)

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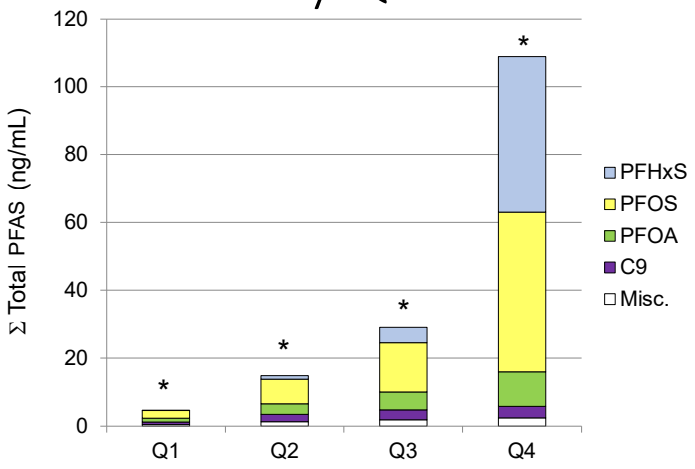
Major PFAS analytes in cat serum by Quartile



*All groups were sig. different from each other in terms of the Σ Total PFCs (ng/mL) (as assessed by ANOVA (Bonferroni post hoc) correction of the ln transformed data).

(Bost *et al* Env Res).

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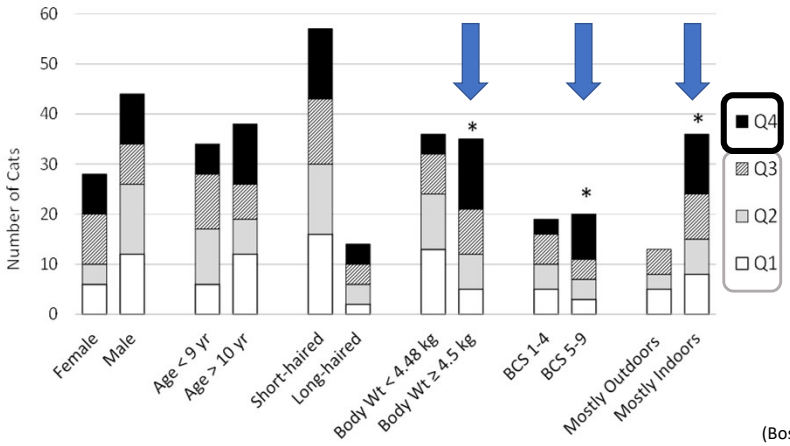
Cat characteristics by quartile as Q_1, Q_2, Q_3, and Q_4 (n =18/quartile) based on total serum PFAS concentrations



*Indicates disproportionately greater numbers of cats with this **factor** in Q_4 vs. Q_{1-3}.

(Bost *et al* Env Res).

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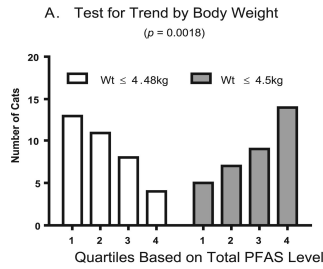
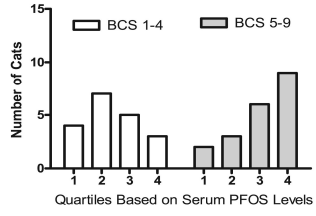
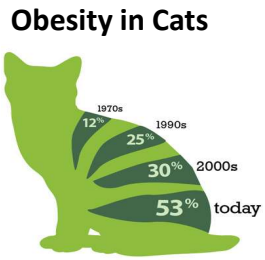
Q4 Cats were Fatter

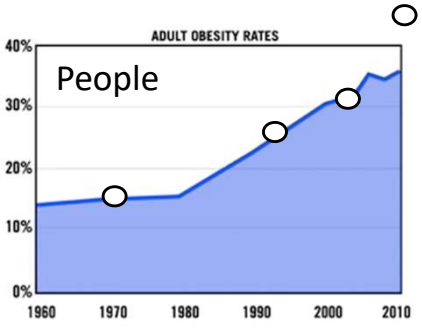




(Bost *et al* Env Res).



http://www.catalystcouncil.org/enewsletter/october2011/



https://lanekenworthy.net/2012/05/31/why-the-surge-in-obesity/

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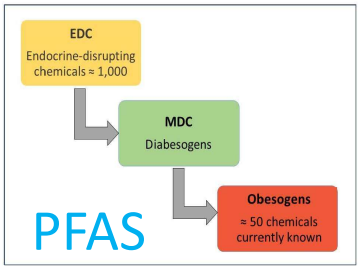
Obesogens

- Promotes "obesity"
- Disturbs insulin signaling in the liver, fat, and muscle cells, ultimately leading to pancreatic dysfunction, insulin resistance, DM
- Disturb thyroid hormone signaling
- Windows of susceptibility
- The most sensitive time period is during fetal development and within the first few years of life.



Suspected obesogens
by *in vitro* and *in vivo* experiments.

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Health Associations of PFAS In Humans

EXPOSURE HAS BEEN LINKED TO

KIDNEY AND TESTICULAR CANCER

HIGH CHOLESTEROL **Metabolic / Liver Disease**

ABNORMAL THYROID HORMONE LEVELS

PREGNANCY-INDUCED HYPERTENSION AND PRE-ECLAMPSIA

OBESITY

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Associations of PFAS In Cats ?

KIDNEY AND TESTICULAR CANCER

HIGH CHOLESTEROL Metabolic / Liver Disease

ABNORMAL THYROID HORMONE LEVELS

PREGNANCY-INDUCED HYPERTENSION AND PRE-ECLAMPSIA

OBESITY

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Associations of PFAS In Cats ?

KIDNEY AND TESTICULAR CANCER

Total PFAS, PFOS & PFHxS HIGH CHOLESTEROL Liver Disease

PFOA ABNORMAL THYROID HORMONE LEVELS Feline HT

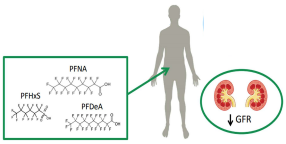
PREGNANCY-INDUCED HYPERTENSION AND PRE-ECLAMPSIA

OBESITY

Total PFAS & PFHxS RESPIRATORY EFFUSIONS

PFOA and PFHxS (trends) KIDNEY DISEASE

(Bost *et al* Env Res).



Blake B *et al Env Pollut* 2018

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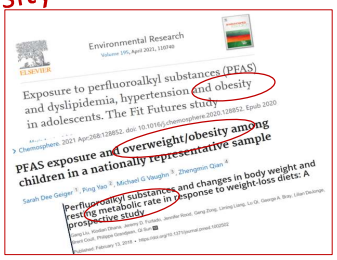
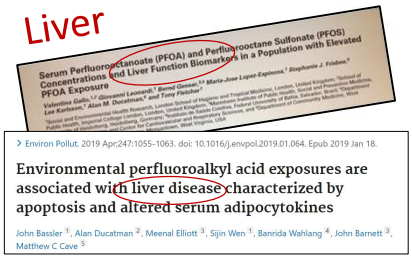
Health associations in humans

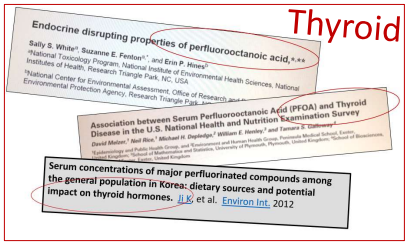
Obesity



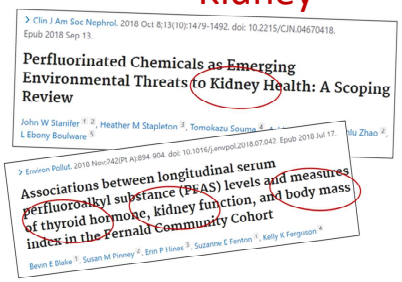
Liver



Thyroid



Kidney



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PBDEs

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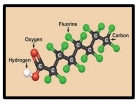
PFAS



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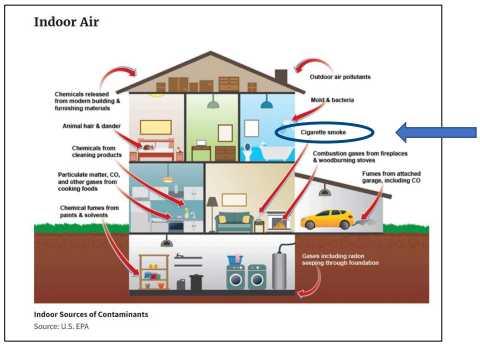
Indoor Products:



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2020 | OriginalPaper | Chapter

4. Role of Pet Dogs and Cats as Sentinels of Human Exposure to Polycyclic Aromatic Hydrocarbons

Authors: Cristian Rial-Berriel, Luis Alberto Henríquez-Hernández, Octavio P. Luzardo

PAHs

Secondhand smoke causes cancer in people

Secondhand smoke is known to cause cancer. It has more than 7,000 chemicals, including at least 70 that can cause cancer.

SHS causes lung cancer, even in people who have never smoked. There's also some evidence suggesting it might be linked in adults to cancers of the:

- Larynx (voice box)
- Nasopharynx (the part of the throat behind the nose)
- Nasal sinuses
- Breast

American Cancer Society

Exposure of mothers and babies to SHS is possibly linked to certain childhood cancers:

- Lymphoma
- Leukemia
- Brain tumors

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Pets and SHS

- Dogs: ↑ risk of lung cancer
  - brachy- and mesocephalic dogs (Reif JS *et al* 1992)
- Dogs: ↑ risk of nasal cancer
  - dolichocephalic dogs (Reif JS *et al* 1998)
- Cats - ↑ risk of malignant lymphoma (Bertone ER et al 2002)

Routes of Exposure

- inhalation (1st hand) X
- inhalation (2nd hand) Dogs & Cats
- oral (3rd hand) Cats via grooming

Secondhand (and Third-Hand) Smoke May Be Making Your Pet Sick

U.S. FOOD & DRUG ADMINISTRATION

What's Lingering on Your Rug, Furniture … ?

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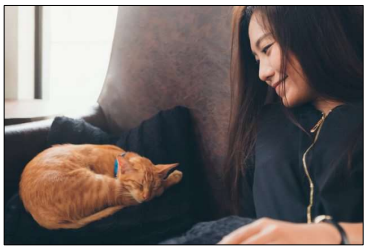
Pets and people share indoor exposures

- With 50 million domestic cats and 80 million dogs occupying ≥ 50 % of homes in the U.S.
- Pets may represent an underutilized resource
- Explore lower-level but chronic exposure and effect relationships in defined environments
- Contribute to the totality of scientific evidence
- Gain improved understanding of shared environmental exposures
- Improving "Health" for humans and pets alike.
- Challenge – design and perform transdisciplinary approaches to address data gaps
- Newer technology – non-targeted analyses

https://www.cdc.gov/healthypets/pets/cats.html



https://en.wikipedia.org/wiki/One_Health_Model

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Thank you for your time.

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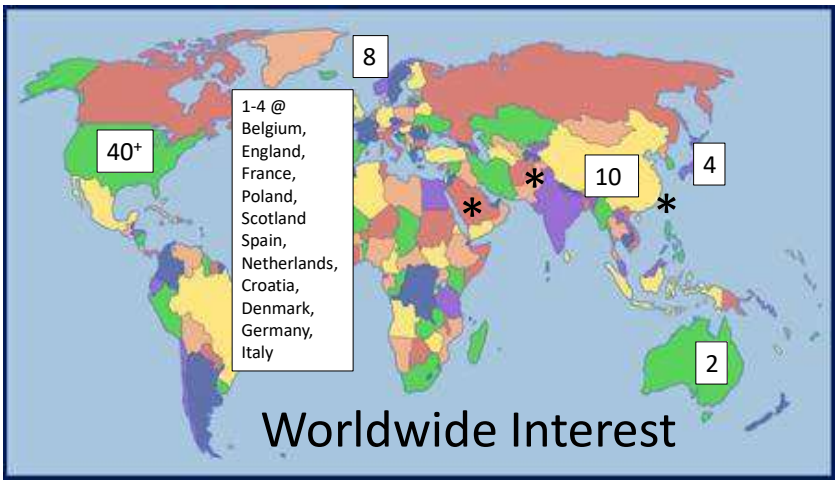
POPs & Pets > 90 publications



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