Analysis of PBDEs in Canine Placental Tissues: Pet Dogs as a Model For Diseases of Developmental Origin

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ABSTRACT

Early life exposures to endocrine disrupting chemicals such as, polybrominated diphenyl ethers (PBDEs) can disrupt crucial developmental processes leading to chronic health issues later in life such as neurodevelopmental disorders and diabetes. Gestation is a critical window for development and the placenta is increasingly recognized as a key player in mediating fetal exposures to environmental contaminants. Previous human studies have shown that PBDEs accumulate in the placenta in a sex- and tissue-specific manner. Understanding the later-life consequences of early life exposures can be challenging due to the long latency periods for chronic human diseases. Pet dogs offer a unique opportunity to serve as a sentinel species for human environmental health studies because they share our environment, have similar genomes and diseases with similar clinical and biological features. Importantly, dogs have a significantly reduced lifespan compared to humans, offering an accelerated path to investigate environmental exposures in utero and their potential associations with health outcomes that stem from developmental origins. We have previously demonstrated that people and their pet dogs have significant and positive correlations in their exposure to PBDEs in indoor environments. Our objective in this study is to demonstrate that pet dogs can act as a sentinel species to evaluate real-world environmental exposures in placental tissues. During the summer and fall of 2021, we collected 22 placenta samples from routine cesarean sections from five different dog litters. Preliminary data from one placenta sample revealed the presence of PBDEs in canine placenta at a concentration of 0.8 ng/g and TBB at a concentration of 0.1 ng/g. Interestingly, we observed higher concentrations of BDE-209 in the fetal placenta tissue compared to maternal placenta tissue, which is similar to trends in human placenta. Our hypothesis is that sex-dependent and tissue-specific accumulation of PBDEs observed in human placental tissues is a conserved phenomenon and would be also found in canine placentas. Dogs are increasingly recognized for their value in translational research in cancer and aging, and thus we think are likely to offer similar value for chronic conditions of developmental origin.

Do dogs accumulate PBDEs in placental tissues with the same trends observed in humans?

INTRODUCTION

Exposure to PBDEs is an environmental health concern for humans and pet dogs

- Polybrominated diphenyl ethers (PBDEs) are a major class of brominated flame retardants used extensively in furniture, electronics and building materials
- Due to environmental persistence and health concerns they were phased out of use in the production of new materials[1]
- Products containing these chemicals still exist in homes
- PBDEs are frequently detected in biological tissues from people[2-4] and dogs[5-8]
- Exposure to PBDEs has been associated with numerous health effects in humans including, endocrine disruption, developmental and carcinogenic effects[1,2]
- Health endpoints related to PBDE exposure in dogs are limited[8]
- PBDEs have been shown to accumulate in placental tissues in a tissue-specific and fetal sex-dependent manner[3,4]

INTRODUCTION

	Hemotrichorial	Hemomonochorial	Endothelialchorial
Life expectancy (years)	2-3.5	72-73‡	10-13*
Average litter size (n)	10-11	1	5-6*
Gestation period (days)	22	270	61
Gross morphology	Discoid	Discoid	Zonary

Histological morphology

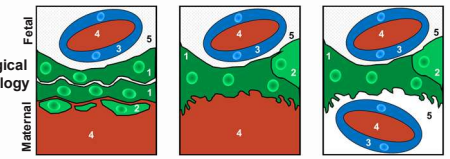

Figure 1. Comparative placentation and gestation between rat, human and dog
The placenta is a transient organ that has a conserved primary function across mammals despite the diversity in gross shape, histological structures and materno-fetal interdigitation. However, these differences do not play a major role in the placental transfer of most chemicals. Ultimately, there is no perfect model organism for human placentation.

‡United Nations global 2019-2020 estimate *variable by breed size; 1. Syncytiotrophoblast 2. Cytotrophoblast 3. Endothelium 4. Blood 5. Interstitium (Adapted from[9]).

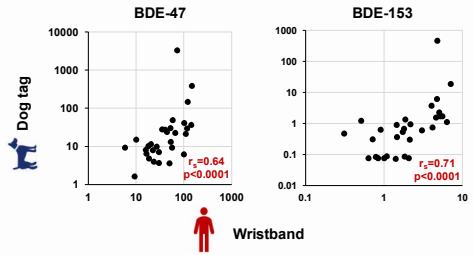

Figure 2. Example scatterplots and Spearman's correlation coefficients (rs) for PBDEs (ng/g) quantified human wristbands and dog tags

We previously demonstrated that humans and dogs living in the same household have shared and similar exposures for many classes of chemical contaminants, including polybrominated diphenyl ethers (PDBEs). Positive and significant Spearman correlations were observed between nearly all brominated flame retardants detected in >50% of human and dog tag samples. Correlations between humans and dogs for BDE-209 could not be calculated due to low detection frequencies[10].

Chemical	r_s	p-value
BDE 28,33	0.78	<0.0001
BDE 47	0.64	0.0001
BDE 100	0.54	0.002
BDE 138	0.39	0.03
BDE 153	0.71	<0.0001
BDE 154	0.60	0.0004
BDE 181	0.15	0.43
TBB	0.75	<0.0001
TEBP	0.37	0.04

STUDY DESIGN

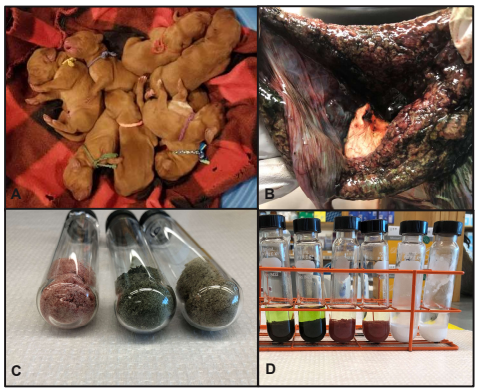

Figure 3. Placenta tissue collection and processing
Dog placenta tissues were obtained from whole litters at veterinary hospitals during routine or medically necessary caesarean sections. (A) litter of new born puppies (B) gross image showing the discoid shape of a dog placenta. The fetal and maternal layers are separated. To show a comparison of placenta tissues from human and dog placentas, tissues are homogenized with sodium sulfate (C) and then solvent extracted for PBDEs (D). Note the intense green color associated with the dog placenta tissues is due to high concentrations of biliverdin. Sodium sulfate alone was used as a lab blank. Following extraction samples are purified with column chromatography then analyzed using gas chromatography/electron-capture negative-ionization mass spectrometry.

PRELIMINARY RESULTS

Litter ID	Total placentas (n)	Male puppies (n)	Female puppies (n)	Breed	Maternal age (years)	Pregnancy number
A	4	1	3	Portuguese water dog	4	2nd
B	2	1	1	Pocket Bully	1	1st
C	5	2	3	Bulldog	1.5	1st
D	6	1	5	French bulldog	2	2nd
E	5	3	2	French bulldog	3	3rd

Table 1. Cohort of pet dog litters that placental tissues were collected from via routine or medically necessary caesarean sections at a veterinary hospital.

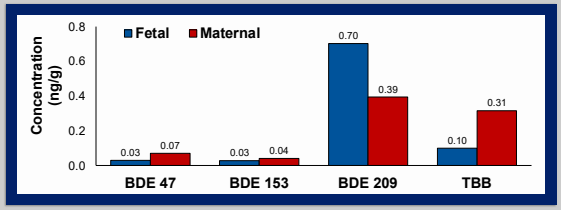

Figure 4. Concentrations of PBDEs and a novel brominated flame retardant in the fetal and maternal layers from a single dog placenta
Data for a few PBDE congeners and the novel brominated flame retardant ethylhexyl tetrabromobenzoate (TBB) were measured in the fetal and maternal layer for a single placenta associated with a female puppy.

INITIAL FINDINGS

- Preliminary data from one placenta sample revealed the presence of PBDEs in canine placenta at a concentration of 0.8 ng/g and TBB at a concentration of 0.1 ng/g
- Higher levels of BDE-209 were present in the fetal tissue compared to the maternal layer, similar to what has been observed in human placentas
- Our hypothesis is that sex-dependent and tissue-specific accumulation of PBDEs observed in human placental tissues is a conserved phenomenon and would be also found in canine placentas

FUTURE DIRECTIONS

We are currently optimizing our analytical methods to include other chemicals, and increase sensitivity to support a lower detection limit

Our primary analyses will have two major endpoints
- Comparison of PBDE accumulation based on fetal sex
- Comparison of PBDE concentrations in the maternal versus fetal layer of dog placentas

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COI STATEMENT

The authors declare no conflicts of interest.

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