The Feline Thyroid Gland: A Model for Endocrine Disruption by Polybrominated Diphenyl Ethers?

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Feline Hyperthyroidism

- Autonomously functional thyroid adenoma(s)
- Analogous to toxic multinodular goiter (TNG)

- Excess thyroid hormones
- Hypermetabolic state
- New York City, 1979
- A geriatric disease
- Most common endocrinopathy in cats
- “Benign” but quality of life is poor
Canned food (2.5-5.64)
- Pop-top cans in males
- Variety of flavors of food (3.8)
- Liver and giblets-flavored food
- Fish-flavored food
- Baby food as kittens (5)
- Lawn and flea products
- Bedding treated with flea products (57.6)
- Exposure to fly sprays (3.3)
- Use of litter box (2.57)
- Indoor housing
- Increased age (1.21/yr)
- Periodontal disease (5.5)
- Female sex (3.3)
- Non-Siamese Breed (0.44)
- Non-Himalayan Breed (0.29)
- Sleeping predominantly on floor (6.6)
- Drinking water from puddles (5.3)
- Regular use of organic fertilizers (5.3)
What are PBDEs?
Polybrominated Diphenyl Ethers

Flame Retardants: Manufactured since 1970s

209 Congeners
3 Commercial Mixtures:
“Penta” “Octa” “Deca”
Where are PBDEs?
PBDE Burdens in Wildlife

Polar Bear ~70 ppb lipid
Harbor seals (Dutch coast) >100 ppb w/w
Sperm whales (Dutch coast) ~100 ppb w/w
Whitebeaked dolphin (Dutch coast) >700 ppb w/w
Beluga whales (Quebec) ~1,000 ppb w/w
Pilot whales (Faroe Islands) 3,160 ppb lipid
Orca/Killer whale (Pacific NW) 8,560 ppb w/w
Bottlenose Dolphins (SE US) 22,780 ppb lipid
*Peregrine Falcon eggs (Sweden) 39,000 ppb lipid
Endocrine Disruptive Properties of PBDEs

Impaired Spontaneous Behavior:
- Decreased Habituation
- Hyperactivity

Altered Learning and Memory

Viberg et al., 2003-2007
Endocrine Disruptive Properties of PBDEs

Thyroid Hormone

Hydroxylated Metabolites of PBDEs
Endocrine Disruptive Properties of PBDEs

Induction of phase I and phase II enzymes (UDPGT)

- Meerts et al., 2000
- Norris et al., 1975
- Stoker et al., 2004
- Kuriyama et al. 2007
- Marsh et al. 1998

Norris et al., 1975
Meerts et al., 2000
Kuriyama et al. 2007
Research Objectives

- Compare PBDE burdens in serum & adipose tissue in age-matched euthyroid vs hyperthyroid cats to determine if hyperthyroidism correlates with higher residues.

- Evaluate the PBDE content of commercial canned cat foods & household dust to identify predominant exposure sources for domestic cats.
Materials and Methods

Silica Gel Chromatography

Sample Extraction: Liquid-liquid/PFE

Gel Permeation Chromatography

GC/HRMS Analysis of Sample Extracts for PBDEs:
Congeners 17, 28, 47, 49, 66, 71, 85, 99, 100, 138, 153, 154, 183, 190, and 209

Lipid Determination: Sulfo-Phospho-Vanillin Reaction
Quality Assurance/Quality Control

- Blanks/Reagent Blanks
- Duplicates
- Spiked samples
  - Surrogates: BDE-118R and 209R
  - Internal standards: FR-250 and BZ209

Accuracy

Precision
Total Serum PBDEs (ng/g lipid)

Client-owned (n = 62)
Range: 370-51,000
Median: 2,615

Euthyroid (n = 21)
Range: 470-16,000
Median: 2,851

Hyperthyroid (n = 41)
Range: 370-51,000
Median: 2,517

Feral (n = 8)
Range: 460-3,700
Median: 759
Total Serum PBDEs (ng/g lipid)

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p = 0.008
Comparison of Log PBDEs (lipid weight) in Serum of Client-Owned Euthyroid (a) and Hyperthyroid (b) Cats vs Age
Research Objectives

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- Evaluate the PBDE content of commercial canned cat foods & household dust to identify predominant exposure sources for domestic cats.
## PBDEs in Commercial Canned Cat Foods

<table>
<thead>
<tr>
<th>Brand and Flavor</th>
<th>ΣPBDEs (ng/g w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fancy Feast Cod, Sole &amp; Shrimp Feast</td>
<td>3.09</td>
</tr>
<tr>
<td>Meijer Main Choice Salmon Dinner</td>
<td>3.01</td>
</tr>
<tr>
<td>Fancy Feast Trout Feast</td>
<td>1.90</td>
</tr>
<tr>
<td>Purina Friskies Pacific Salmon Dinner in Sauce</td>
<td>1.90</td>
</tr>
<tr>
<td>9 Lives Ocean Whitefish Dinner (n = 2)</td>
<td>1.80</td>
</tr>
<tr>
<td>Fancy Feast Tuna in Gravy</td>
<td>1.70</td>
</tr>
<tr>
<td>Fancy Feast Ocean Whitefish &amp; Tuna Feast</td>
<td>1.70</td>
</tr>
<tr>
<td>Meijer Main Choice Ocean Whitefish &amp; Tuna Dinner</td>
<td>0.75</td>
</tr>
<tr>
<td>Purina Friskies Ocean Whitefish &amp; Tuna Dinner</td>
<td>0.42</td>
</tr>
</tbody>
</table>
Summary of Total PBDEs in Dust

Total of Dust Samples (n = 19)
Range: 510-95,000
Median: 1,959

Euthyroid Cats (n = 12)
Range: 510-4,900
Median: 782

Hyperthyroid Cats (n = 7)
Range: 1,100-95,000
Median: 17,177
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Hyperthyroid Cats (n = 7)
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Median: 17,177

p = 0.002
Calculated Daily Intake of PBDEs in Cats

From Canned Food:
Assumes 5 oz of food/day and 5 kg BW
Mean: 51 ng/kg/day
Range: 12-91 ng/kg/day

From Dust:
Assumes 200 mg of dust ingested/day
Mean: 320 ng/kg/day
Range: 20-3,800 ng/kg/day
Both Sources:
Mean: 371 ng/kg/day
Range: 32-3,900 ng/kg/day

At the high end, this represents 1.3% of the lowest single acutely toxic PBDE dose known to disrupt thyroid function in laboratory animals.
Domestic cats are highly exposed to PBDEs with the highest recorded levels on the planet: 51,063 vs previous high of 39,000 ng/g lipid.
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Total PBDE serum burdens do not significantly differ between client-owned euthyroid and hyperthyroid cats.
Conclusions

🌟 Feral cats have significantly lower PBDE burdens in serum than both euthyroid and hyperthyroid client-owned (older) cats.
Conclusions

✦ Feral cats have significantly lower PBDE burdens in serum than both euthyroid and hyperthyroid client-owned (older) cats.

✦ Dust is likely the primary route of exposure of domestic cats to PBDEs.
Feral cats have significantly lower PBDE burdens in serum than both euthyroid and hyperthyroid client-owned (older) cats.

Dust is likely the primary route of exposure of domestic cats to PBDEs.

Total PBDEs were significantly higher in dust from homes of hyperthyroid cats versus homes of euthyroid cats.
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MAYBE
Future Research

ADME:
Half-life studies
Enzyme Induction

TR Effects:
RC3/Neurogranin

Thyroid Effects:
cAMP mRNA
Broader Implications
THANKS!!!

My Committee:
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Dr. Thomas Graves

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