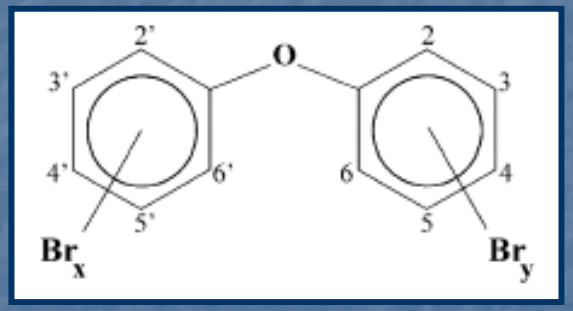
The ABCs and PBDEs of Feline Hyperthyroidism: Current Findings on a Modern Epidemic



Donna Mensching, DVM, MS, DABVT, DABT
May 8, 2009

Feline Hyperthyroidism

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

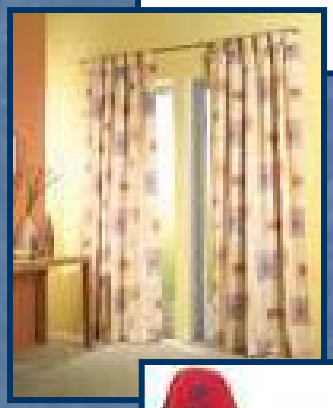
- Excess thyroid hormones
- Hypermetabolic state
- New York City, 1979
- A geriatric disease
- Most common endocrinopathy in cats
- “Benign” but quality of life is poor

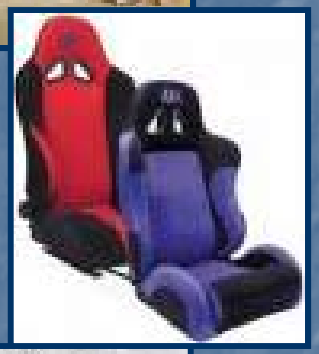
Epidemiologic Risk Factors for Feline Hyperthyroidism

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)

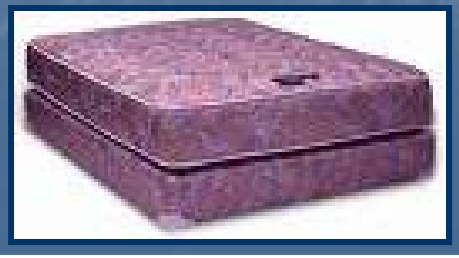
Where are PBDEs?







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

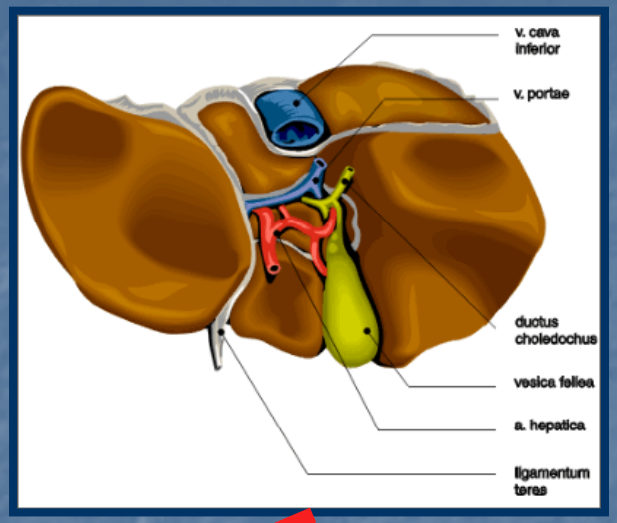
Pilot whales (Faroe Islands) 3,160 ppb lipid

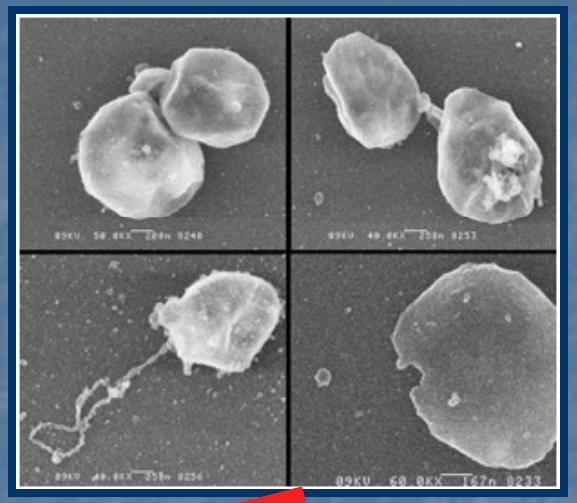
Orca/Killer whale (Pacific NW) 8,560 ppb w/w

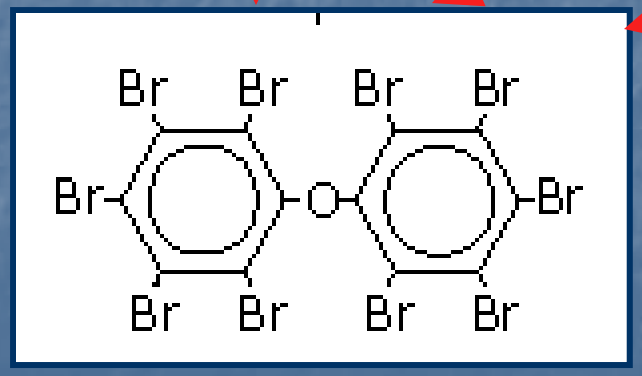
Bottlenose Dolphins (SE US) 22,780 ppb lipid

***Peregrine Falcon eggs (Sweden) 39,000 ppb lipid**

Environmental and Biologic Fate of PBDEs







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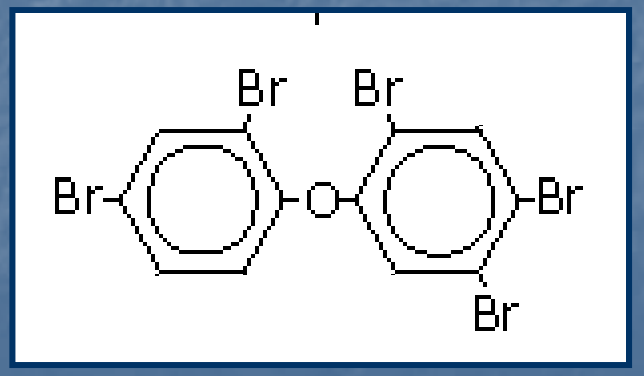

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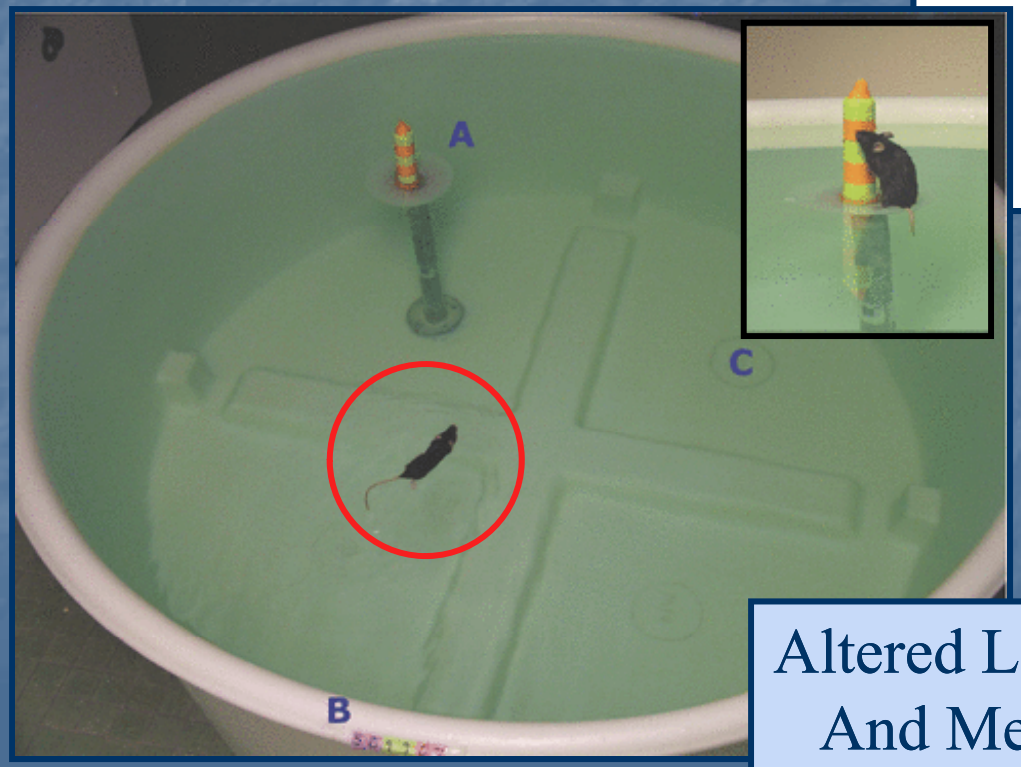
Endocrine Disruptive Properties of PBDEs

Impaired Spontaneous Behavior:
Decreased Habituation
Hyperactivity

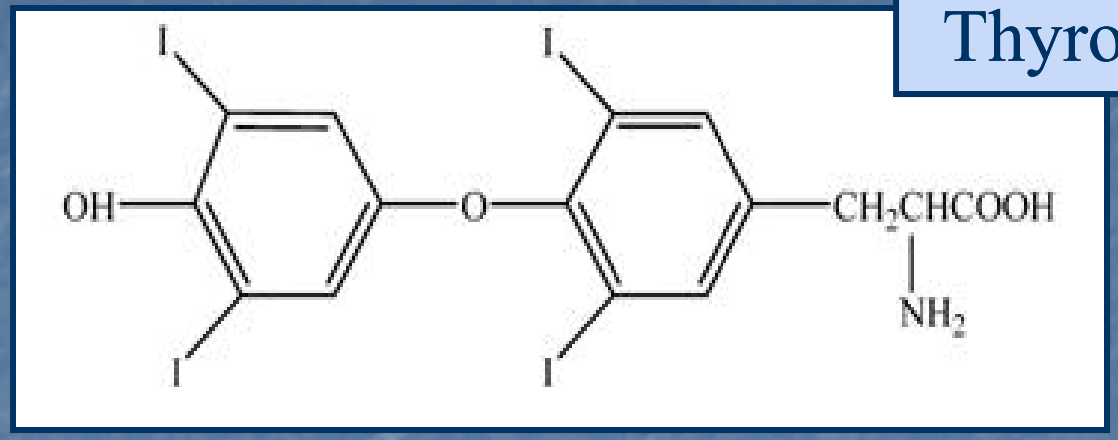


Altered Learning
And Memory

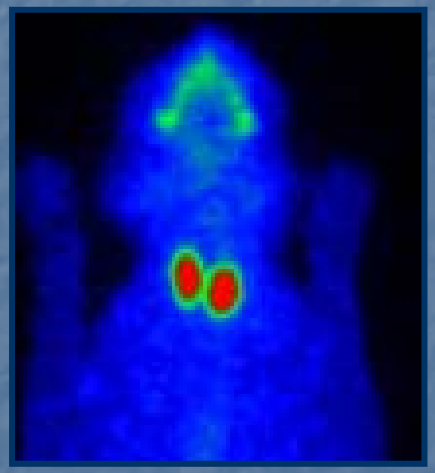
Viberg et al., 2003-2007

Endocrine Disruptive Properties of PBDEs

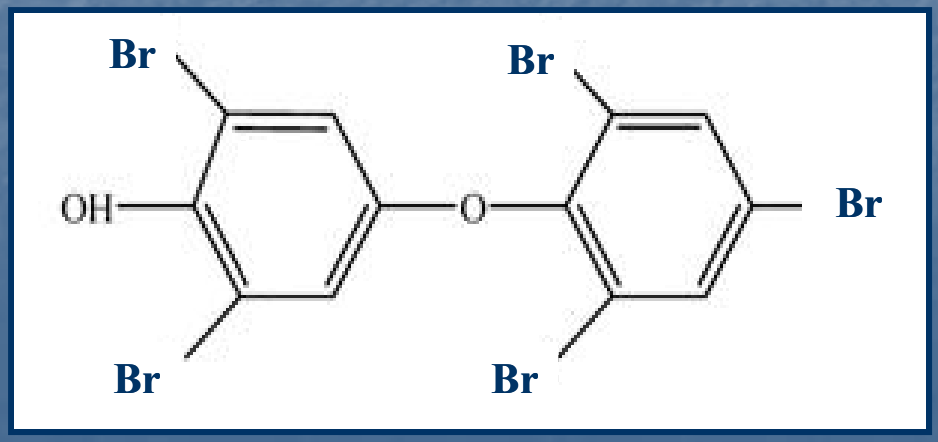
Thyroid Hormone



VS



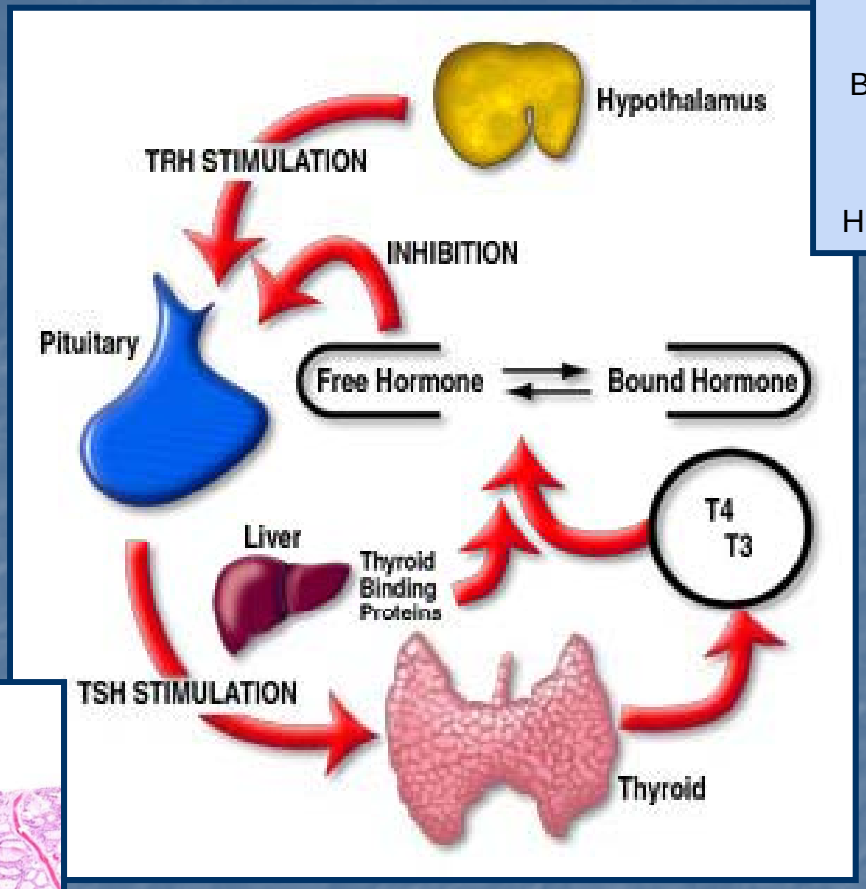
Hydroxylated Metabolites of PBDES

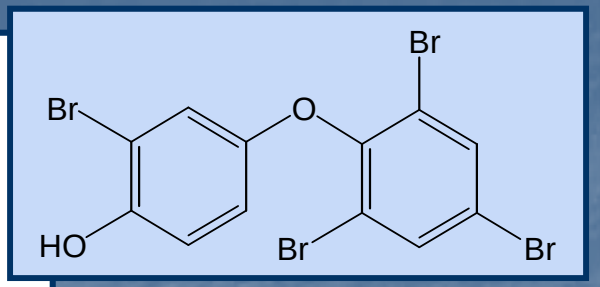


Endocrine Disruptive Properties of PBDEs

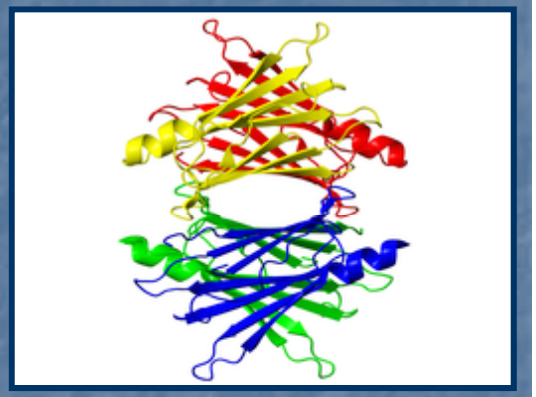
Induction of phase I and phase II enzymes (UDPGT)

Stoker et al., 2004

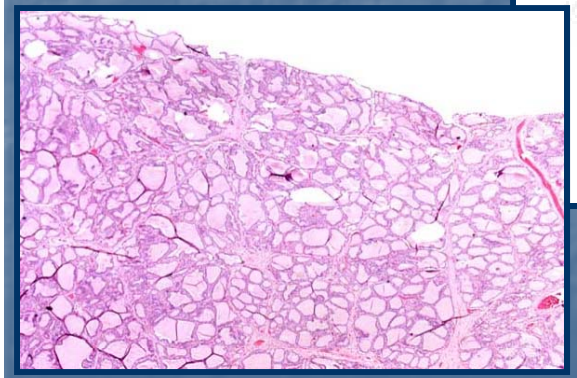




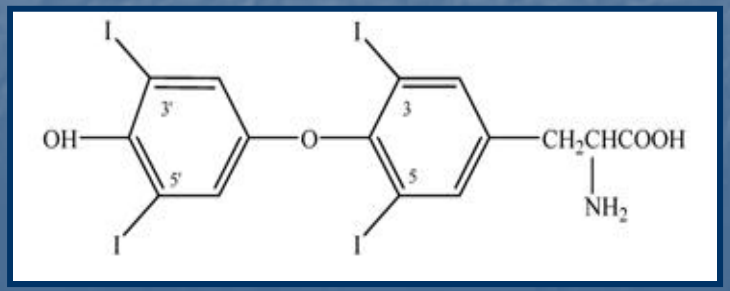
Marsh et al. 1998



Meerts et al., 2000



Norris et al., 1975



Kuriyama et al. 2007

PBDEs and Hyperthyroidism

Elevated PBDE Levels in Pet Cats: Sentinels for Humans?

Dye et al. 2007

Groups	ΣPBDE (42) congeners in serum
Young (n = 5):	4.3 +/- 1.5 ng/ml (median of 3.5)
Old non-HT (n = 7):	10.5 +/- 3.5 ng/ml (median of 5.9)
HT (n = 11):	12.7 +/- 3.9 ng/ml (median of 6.2)

Conclusions: High variability between groups with no association between HT cats and PBDE levels

PBDE levels in cats are 20-100X greater than median levels in U.S. adults (2003)

Cat food Analyses

Canned: 0.17 - 1.75 ng/g wet weight

Dry: 0.6 - 2.9 ng/g wet weight

Canned food eaters had a greater proportion BDEs-47 and 99

Dry food eaters had the greatest proportion of BDE-209

Research Objectives

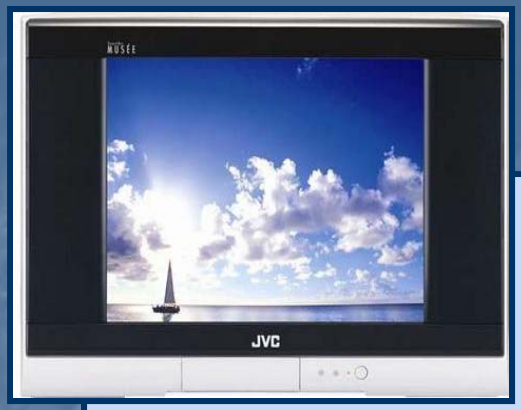
- Identify epidemiologic risk factors for development of FH through a brief client survey

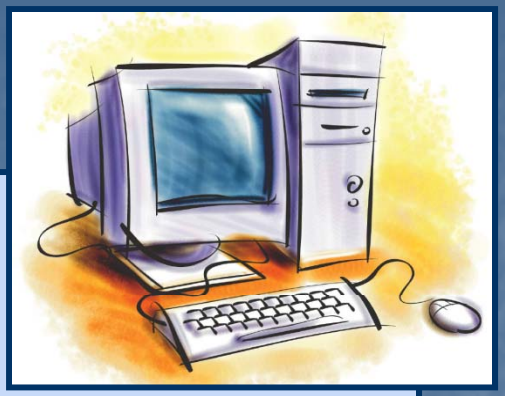
- Validate a TSH assay for cats to identify a subset of euthyroid cats with elevated TSH concentrations & correlate TSH concentrations with PBDE burdens in serum

- 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

Client Survey Results





Total Questionnaires = 19
Hyperthyroid homes = 9
Euthyroid homes = 10

% of time indoors: 95%
# of cats in the home: 3.6
# of litter boxes: 2.5
% of canned food in diet: 40.4%
# of televisions: 1.6
# of computers: 1.6
Frequency of vacuuming: q ~10 days

Conclusions: Distributions in hyperthyroid vs euthyroid groups did not differ with any factor

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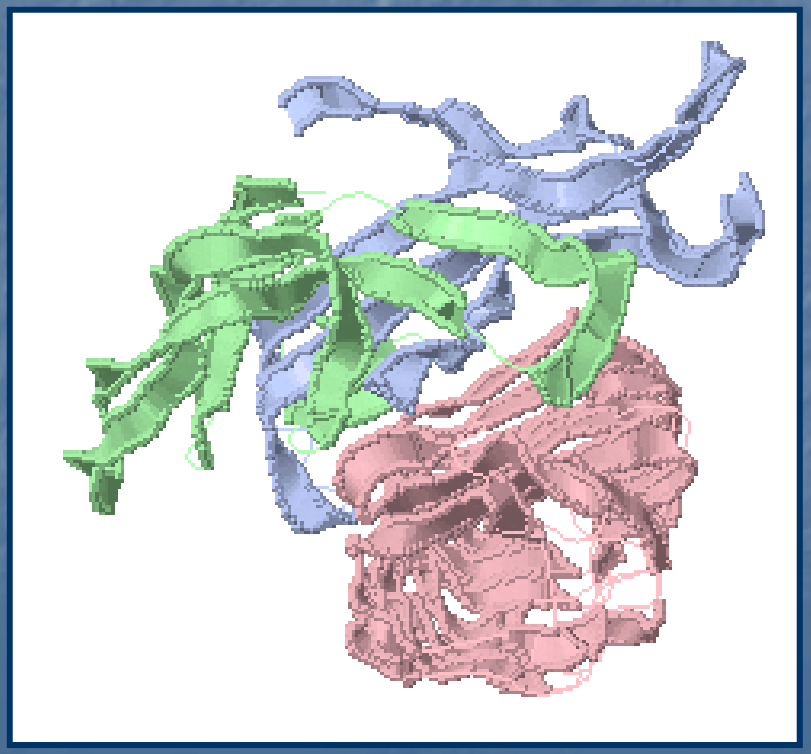
TSH Validation

Feline recombinant TSH
Canine DPC chemiluminescent assay

Feline Cross-reactivity: 35.7%

Detection Limit:
0.03 ng/ml



$r^2 = 0.992$

Rayalam et al., 2006

Summary of Serum TSH Results

Study Group	Measured TSH (ng/ml)
*Client-owned/euthyroid cats (n = 18)	5 detectable (mean: 0.038) 13 undetectable (< 0.03)
*Client-owned/hyperthyroid cats (n = 36)	100% undetectable
Feral euthyroid cats (n = 9)	1 detectable (0.11) 8 undetectable

*$p < 0.01$

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Materials and Methods

Sample Extraction:
Liquid-liquid/PFE

Silica Gel Chromatography

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

Total Serum PBDEs (ng/g lipid)

Client-owned
(n = 62)
Range: 373-51,063
Mean: 5,865
Median: 2,615

Euthyroid
(n = 21)
Range: 467-15,949
Mean: 5,263
Median: 2,851

Hyperthyroid
(n = 41)
Range: 373-51,063
Mean: 6,173
Median: 2,517

Feral
(n = 8)
Range: 457-3,712
Mean: 1,203
Median: 759

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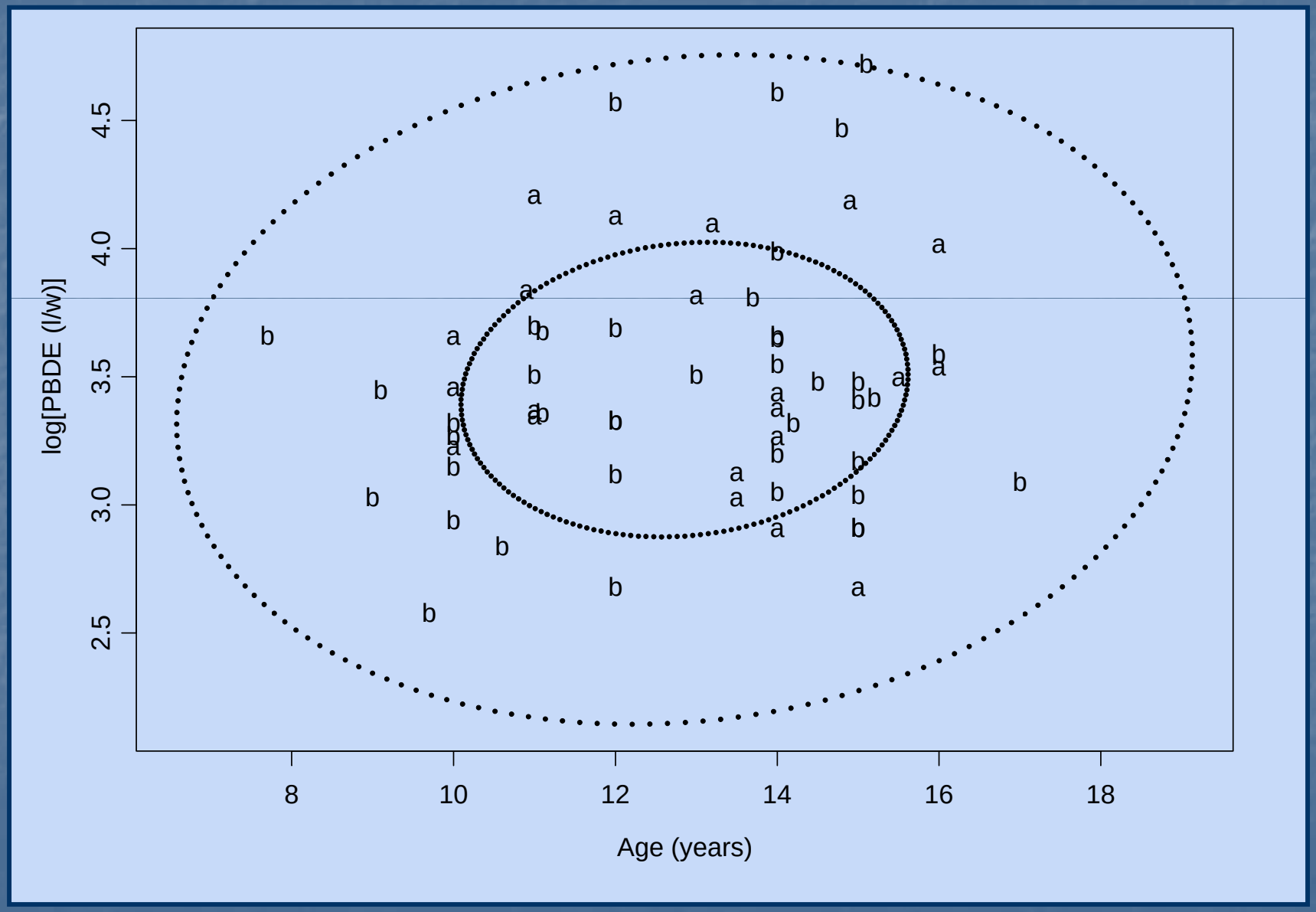
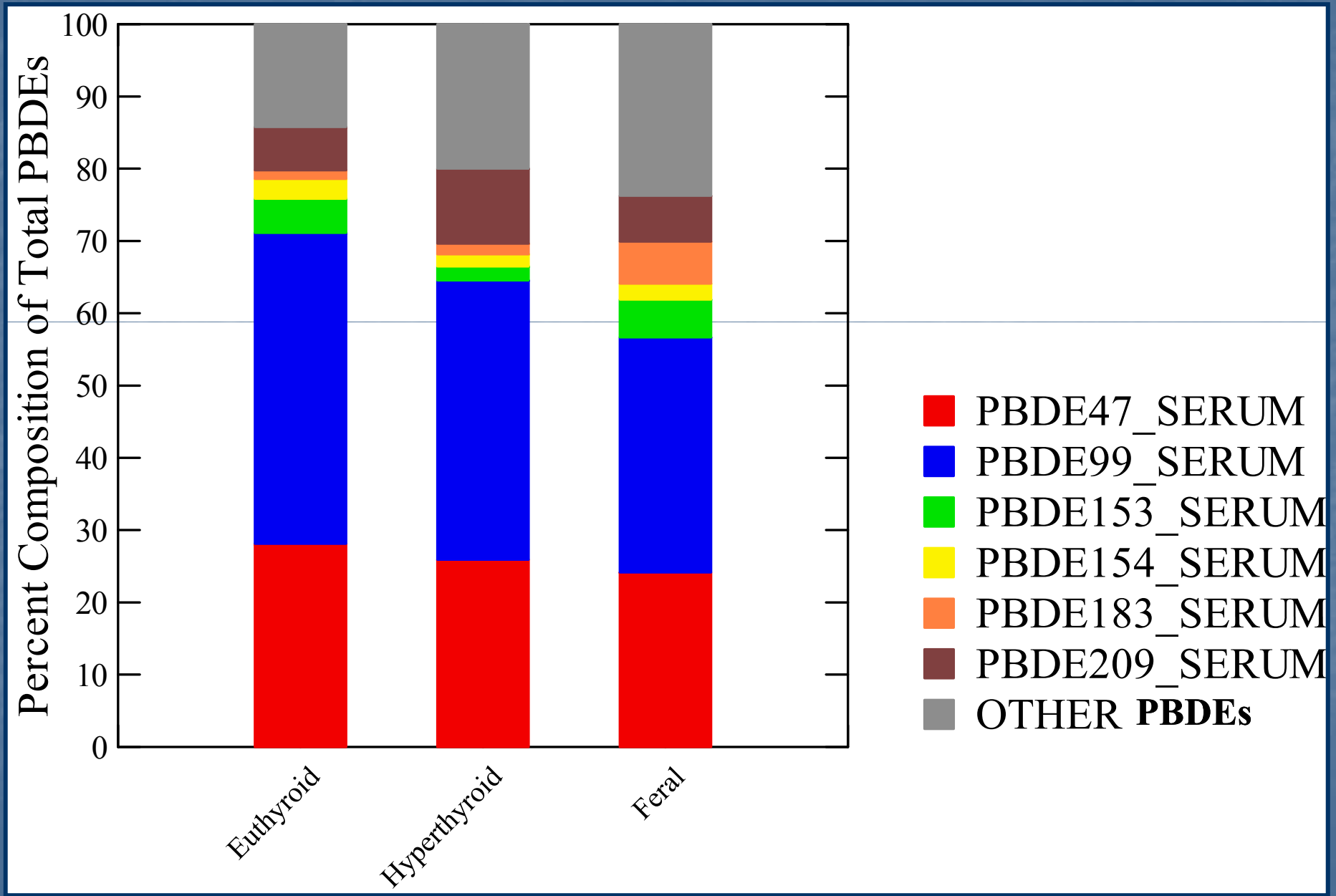
$p < 0.01$

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



Percent Composition of PBDEs in Serum



Total PBDEs in Adipose Tissue

ΣPBDEs (ng/g lipid)
79
295
417
860*
4753

Mean: 1281
Median: 417
*Hyperthyroid

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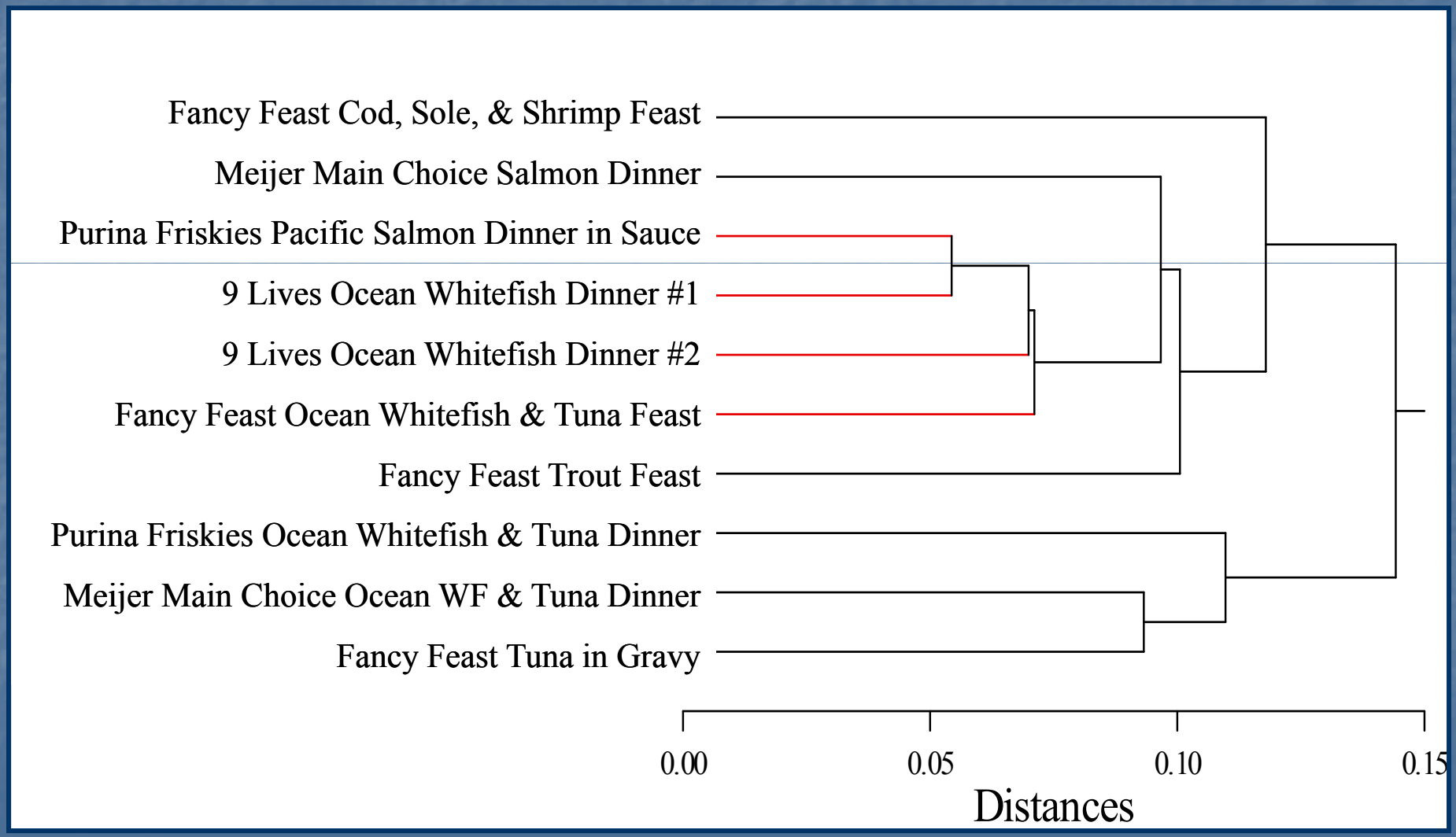
PBDEs in Commercial Canned Cat Foods

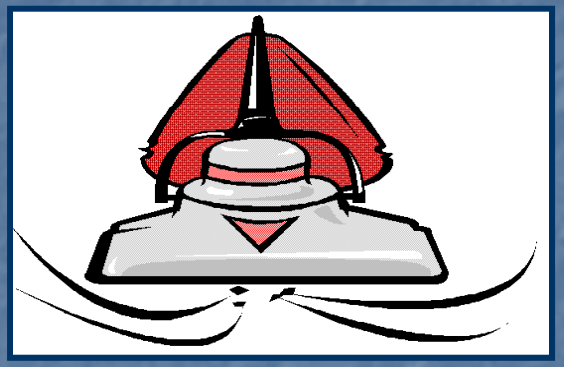
Brand and Flavor	ΣPBDEs (ng/g w/w)
Fancy Feast Cod, Sole & Shrimp Feast	3.09
Meijer Main Choice Salmon Dinner	3.01
Fancy Feast Trout Feast	1.90
Purina Friskies Pacific Salmon Dinner in Sauce	1.89
9 Lives Ocean Whitefish Dinner (n = 2)	1.76
Fancy Feast Tuna in Gravy	1.69
Fancy Feast Ocean Whitefish & Tuna Feast	1.65
Meijer Main Choice OceanWhitefish & Tuna Dinner	0.75
Purina Friskies Ocean Whitefish & Tuna Dinner	0.42

Cluster Analysis of Commercial Canned Cat Foods



Summary of Total PBDEs in Dust

Total of
Dust Samples
(n = 19)
Range: 510-95,448
Mean: 8,098
Median: 1,959



Euthyroid Cats
(n = 14)
Range: 510-4,911
Mean: 1,698
Median: 1,489

Hyperthyroid Cats
(n = 7)
Range: 1,060-95,448
Mean: 19,372
Median: 3,137

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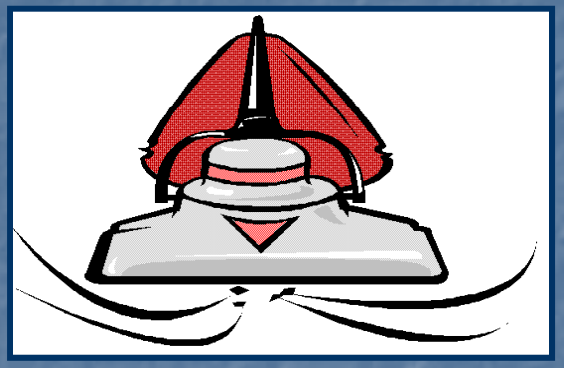

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≠

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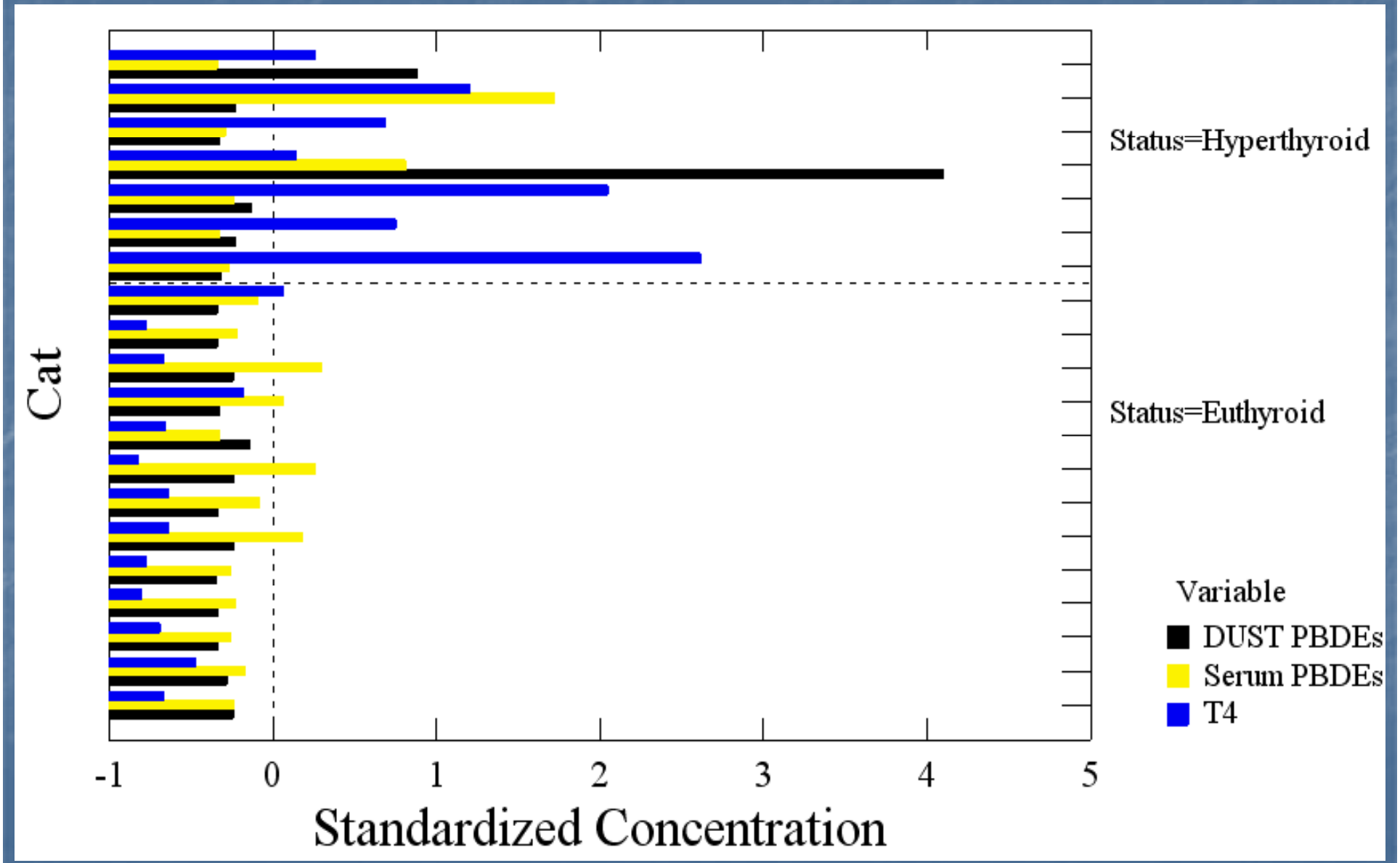
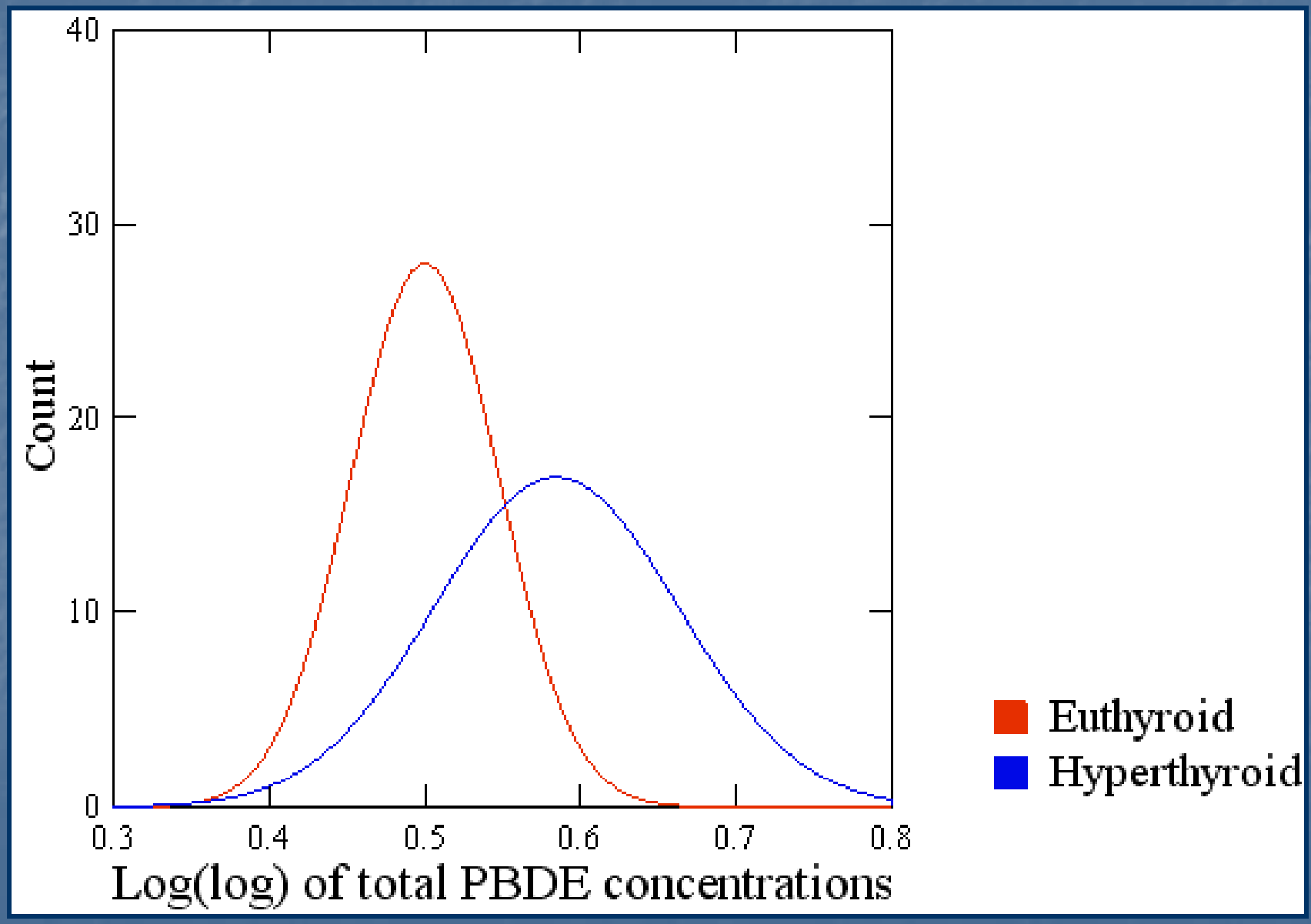
Median: 3,137

p = 0.0183

Serum T4 and Total PBDEs in Serum and Dust in Client-Owned Euthyroid vs Hyperthyroid Cats



Theoretical Distributions of Total PBDEs in Dust from Homes of Euthyroid vs Hyperthyroid Cats



Calculated Daily Intake of PBDEs in Cats

Forward calculation from canned food and dust:

From Canned Food:

Assumes 5 oz of food/day and 5 kg BW

Mean: 51 ng/kg/day

Range: 12-88 ng/kg/day

From Dust:

Assumes 200 mg of dust ingested/day

Mean: 324 ng/kg/day

Range: 20-3,818 ng/kg/day

Calculated Daily Intake of PBDEs in Cats

Both Sources:
Mean: 375 ng/kg/day
Range: 32-3,906 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.

Calculated Daily Intake of PBDEs in Cats

Backward calculation from serum values:
1 ng/g of body burden = 0.177 ng/kg/day

Mean: 1,038 ng/kg/day
Range: 66-9,038 ng/kg/day

At the high end,
this represents 3.0% of the lowest single acutely toxic
PBDE dose known to disrupt thyroid function
in laboratory animals.

PBDEs and Hyperthyroidism

Elevated PBDE Levels in Pet Cats: Sentinels for Humans?

Dye et al. 2007

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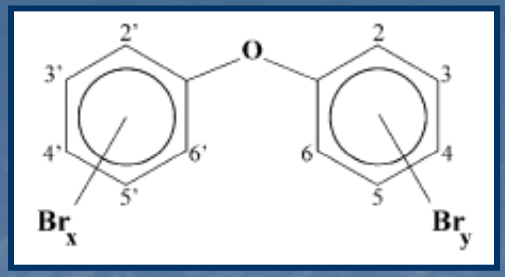
Groups	ΣPBDE (42) congeners in serum
Young (n = 5):	1,720 +/- 600 ng/g lipid (median of 1,400)
Old non-HT (n = 7):	4,200 +/- 1,400 ng/g lipid (median of 2,360)
HT (n = 11):	5,080 +/- 1,560 ng/g lipid (median of 2,480)

Conclusions



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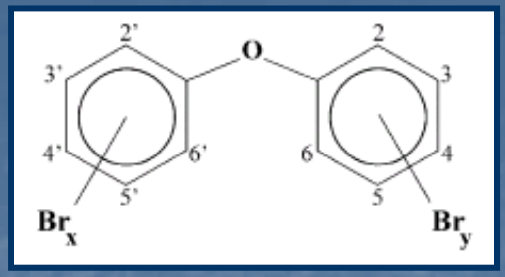
Conclusions



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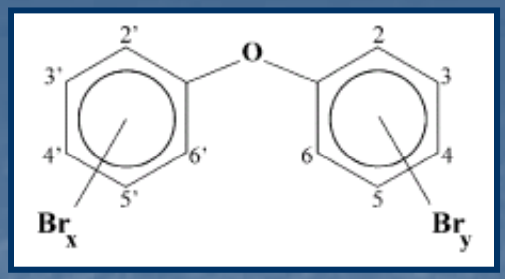

- Domestic cats are highly exposed to PBDEs with the highest recorded levels on the planet: 51,063 vs previous high of 39,000 ng/g lipid

- In the cats studied, TSH was not elevated in relation to PBDE residues.

- 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.

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- 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.

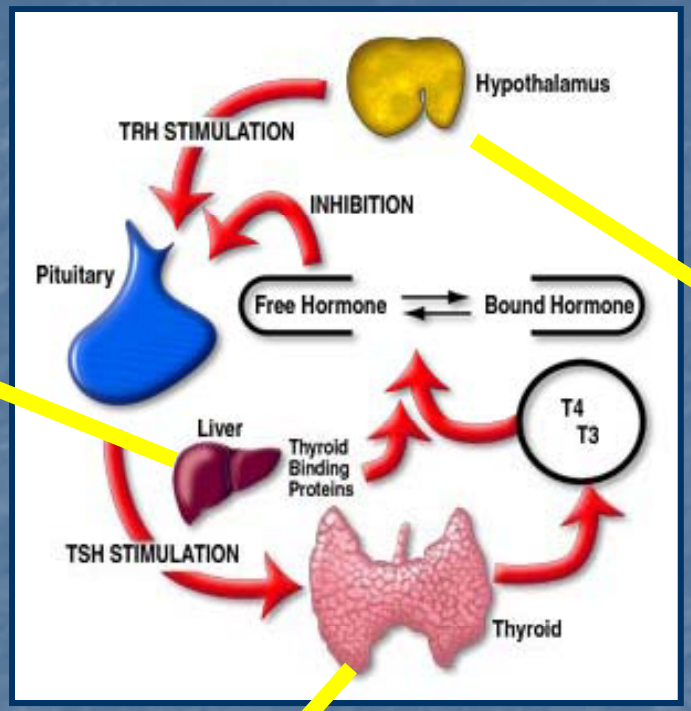
- Total PBDEs were significantly higher in dust from homes of hyperthyroid cats versus homes of euthyroid cats.

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

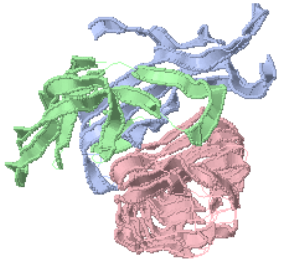
The Feline Thyroid Gland: A Model for Endocrine Disruption by Polybrominated Diphenyl Ethers?

MAYBE

Future Research

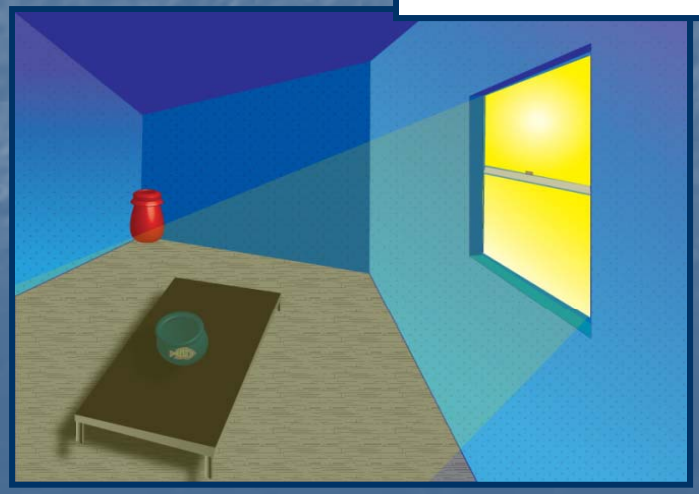


TR Effects: Developmental TR α vs β

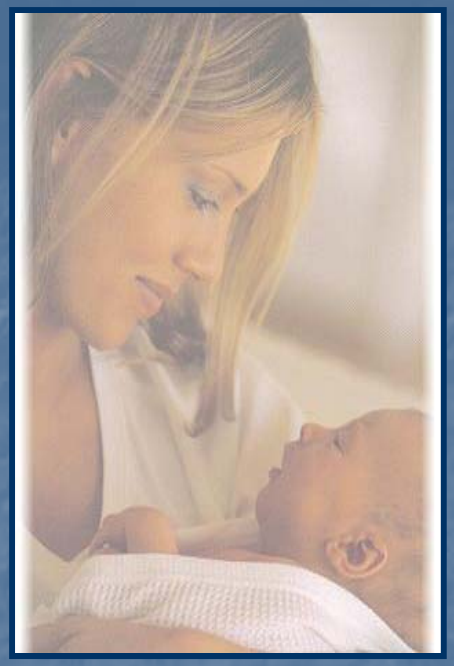


Pharmacokinetics: Half-life studies Enzyme Induction

Thyroid Effects: cAMP mRNA



Broader Implications



Thank you
for your attention!

ILLINOIS SUSTAINABLE TECHNOLOGY CENTER
UNIVERSITY OF ILLINOIS AT URBANA-CHAMPAIGN

http://www.istc.illinois.edu/info/library_docs/RR/RR-115.pdf

Questions?