

Flame Retardants and Human Health: Effects on Thyroid and Reproductive Hormones

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Overview

- Thyroid hormones, reproductive hormones, and diabetes
- Studies of PBDEs and hormones in animals and humans
- New human studies on PBDE exposure and neurological and reproductive health outcomes.

Endocrine Disruption

- Effects of environmental chemicals on the regulation of the endocrine system
 - Interfere with or mimic hormones
 - Possible influences on growth, development and diseases

Age at Exposure is Critical

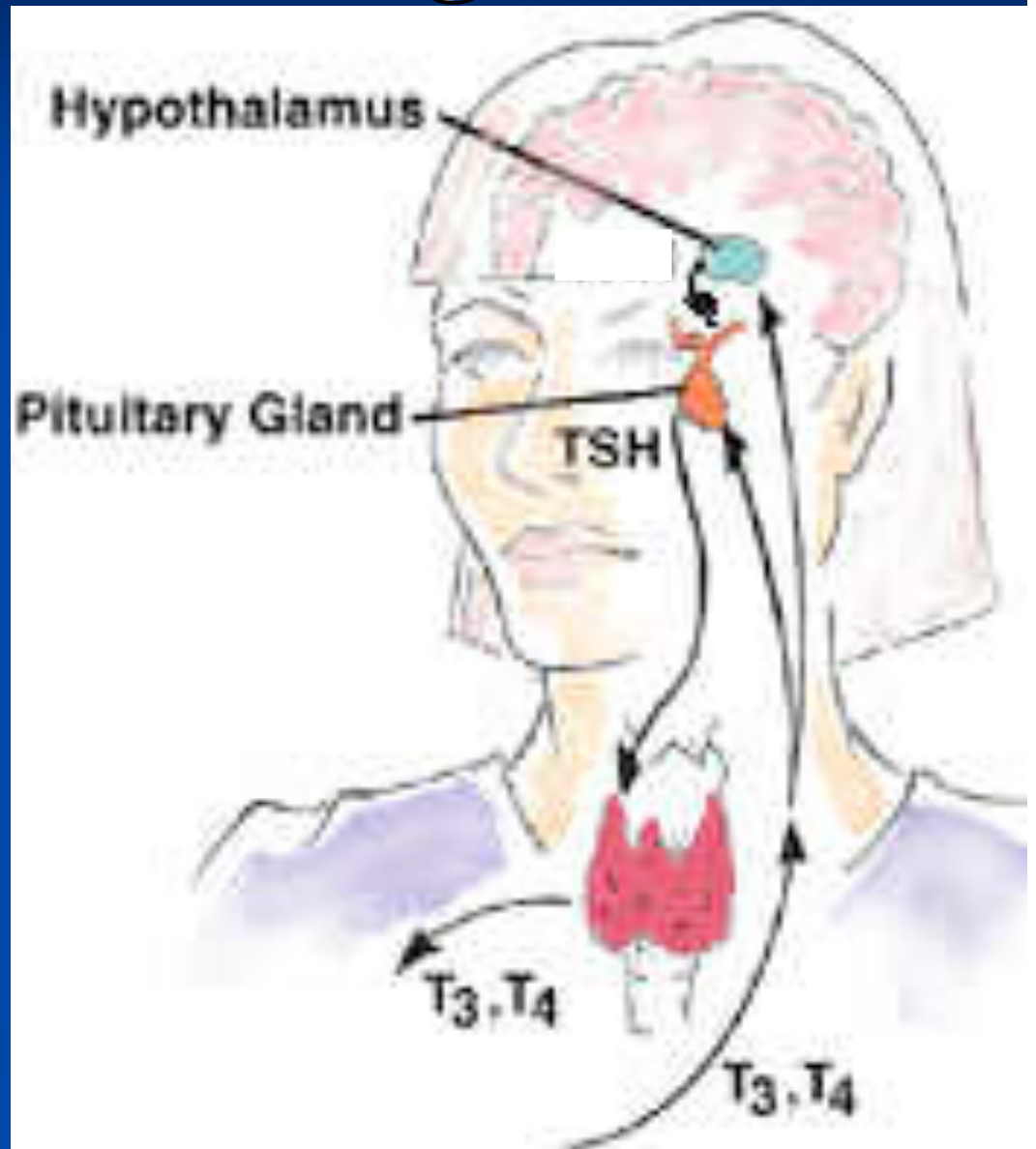
- We are most concerned about early life exposures to endocrine disruptors
 - Hormones control developmental processes
 - Changes during development are irreversible
 - Early life exposures can predispose to adult diseases
- However, later exposures may also lead to disease

We are all exposed to many chemicals

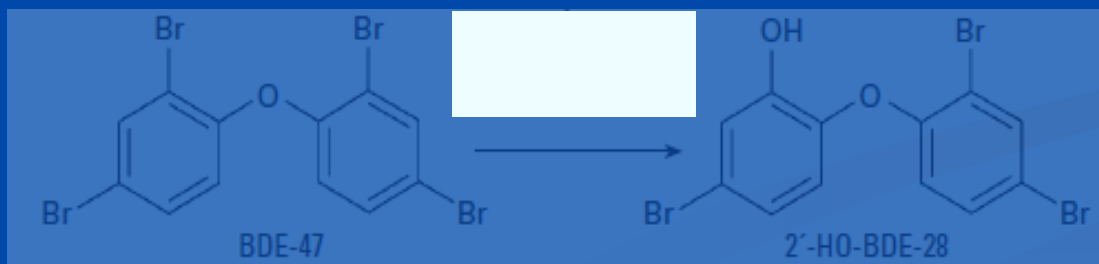
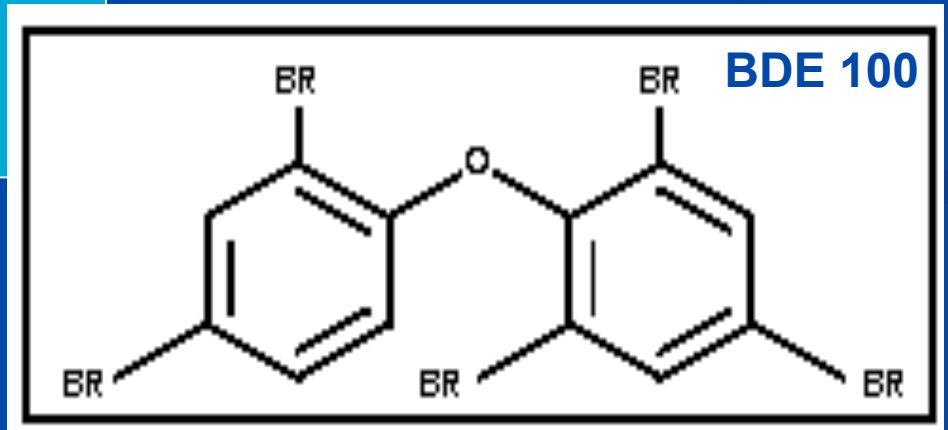
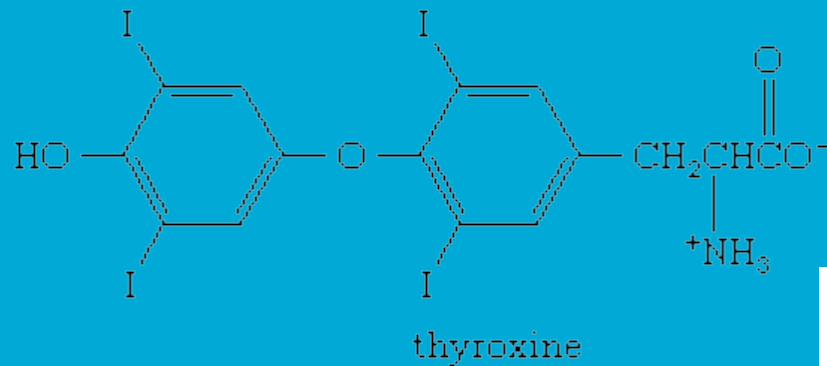
- Potential interactions among chemicals on health outcomes
- We have difficulty studying multiple exposures in humans because many exposures are correlated
- Our exposures are changing over time
 - changes in the types of flame retardant chemicals in products

Thyroid Hormone Regulation

- TSH = thyroid stimulating hormone
- T4 & T3 are 2 hormones made in the thyroid



PBDE & Thyroxine (T4)



Qui et al, Environ Health Perspect 115:1052, 2007

Why are we concerned about thyroid hormones?

1. Developing children

- Thyroid hormone essential for normal brain development
- Fetus doesn't produce thyroid hormone in first trimester
- Moderate maternal thyroid insufficiency → decreased IQ
- Prenatal PBDE exposure has recently been associated with human physical and mental developmental outcomes (Herbstman et al., 2010 and Roze et al., 2009)

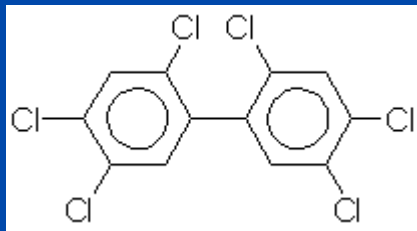
Why are we concerned about thyroid hormones?

2. Adults

- Thyroid disease is common
 - most common in older women
 - many cases are autoimmune disease if sufficient iodine in diet
- Thyroid cancer
 - rare but increasing worldwide

PBDES and Thyroid Hormones: Animals

- Reduction in T4
- No consistent effects on TSH or T3
- PBDE and PCB effects are similar



- PCBs and other chemicals are found in Great Lakes fish
- Frequent and infrequent Great Lakes sport fish consumers
- 4000 residents of IL, IN, WI, MI, OH
- Started in 1993, now in third follow up study
- Directed by Wisconsin Division of Public Health and University of Illinois at Chicago

Exposures



- PCBs and DDE
 - Highest in those eating sport fish for many years
 - Declined over the study
 - PCBs in men are still higher than US population exposure
- PBDEs
 - Related to levels of bromine in sleeping pillow and car upholstery
 - Increased over the study
 - Exposure levels are similar to the US population

Health Effects



- Children born to women who ate sport fish for many years prior to pregnancy or who had higher DDE blood levels had lower birth weights than infants born to other women.
- Diabetes more common in participants with higher levels of DDE in their blood.
- Thyroid
 - PCBs and DDE not associated with clinical thyroid disease
 - PCBs associated with decreased thyroid hormones (T4)—similar to animal studies

Thyroid Hormone Increases with PBDE Exposure in Men



N	304
Total T4	↑
Free T4	↑
Total T3	↓
TSH	↓

Turyk et al., 2008

Thyroid Hormones and PBDEs: U.S. Studies

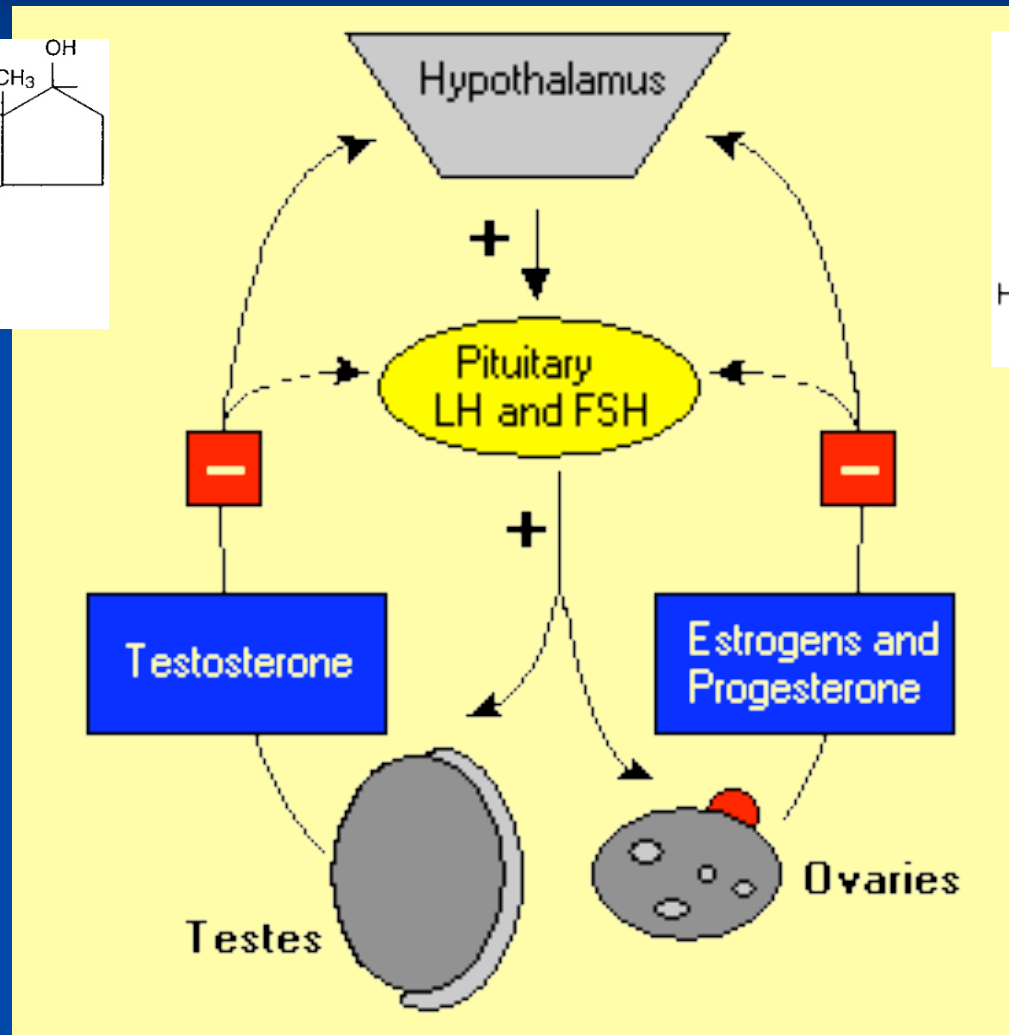
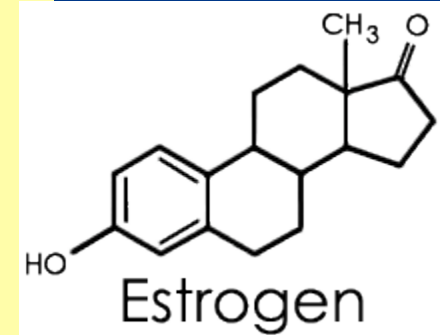
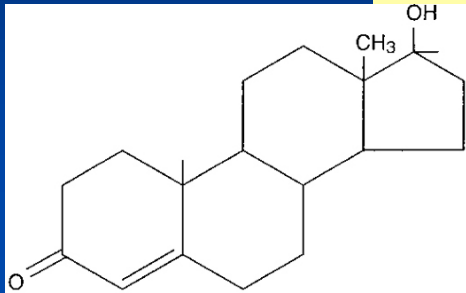
Study	N	Free T4	TSH
Turyk ♂	304	↑	↓
Bloom	36	(↑)	-
Meeker ♂	24	↑	-
Chevrier ♀	287	-	↓



Thyroid Autoantibodies & PBDEs

- Thyroid autoantibodies are very common in patients with autoimmune thyroid disease
- Men with the highest PBDE exposures had 6 times the risk of having thyroid autoantibodies compared with men with lower PBDEs
- Suggests they may have an increased risk of developing thyroid disorders
- New follow up study will look for thyroid disease

Reproductive Hormones



Potential Health Effects Related to Changes in Reproductive Hormones

- Hormonally related cancers
 - Breast, ovarian, prostate
- Endometriosis, uterine fibroids, early menarche, infertility in males and females
- Reproductive outcomes
 - Decreased birth weight
 - Decreased length of gestation
 - Cryptorchidism (undescended testicles)

PBDEs and Human Health

- Congenital cryptorchidism (Main et al 2007)
- Lower birth weight and length (Chao et al 2007)
- Longer time to pregnancy (Harley et al., 2010)
- Decreased sperm concentration and testicular volume (Akutsu et al., 2008)

PBDEs and Reproductive Hormones: Animals

- In rats, PBDE exposure during development and in adults is associated with decreased reproductive hormones
- Developmental exposure to PBDEs at doses comparable to human exposures:
 - Females: decreased estradiol & ovary weight, and thyroid changes (Talsness 2008)
 - Males: hyperactivity & decreased sperm count (Kuriyama 2007)

Reproductive Hormones and PBDEs



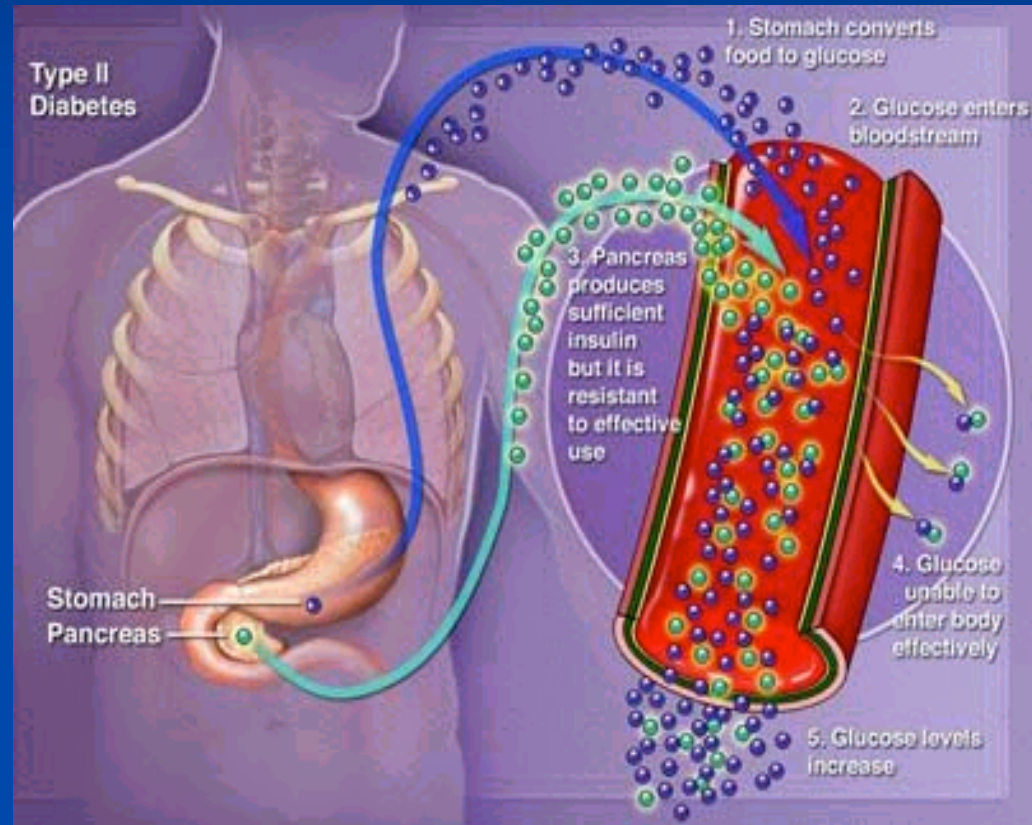
- In Fish Consumers
 - Men: increased testosterone (Turyk et al., 2008)
 - Postmenopausal women: decreased FSH, no change estrogen
- PBDEs in house dust were associated with decreased FSH, LH and free testosterone. (Meeker et al., 2009)

Organophosphate flame retardants in house dust are associated with changes in hormones in men

- TDCPP (chlorinated tris) was associated with decreased free T4 and increased prolactin
- TPP (triphenyl phosphate) was associated with increased prolactin and decreased sperm concentration
- (Meeker and Stapleton 2009)

Diabetes

- Many studies suggest that POPs (PCBs, dioxins, pesticides) are related to diabetes and insulin resistance
- Are PBDEs also associated with diabetes?



PBDEs and Diabetes

- Diabetes was associated with BDE 153 in a large study representative of the U.S. population (Lim et al, 2008)
- Fish consumer cohort (Turyk et al, 2009)
 - Overall, diabetes was not associated with PBDEs
 - But, people who had higher levels of both PBDEs and DDE had the highest risk of diabetes
 - Also, an association of diabetes and PBDEs was found in people with hypothyroid disease
 - New follow up study will explore diabetes incidence after PBDE exposure



Summary

- New human studies are finding associations of PBDE exposure with health outcomes.
- Associations of PBDEs with hormones have been found in human studies, but results are inconsistent.
- Very little health data is available on new flame retardants
- No data is available on health effects of mixtures of PBDEs and newer flame retardants

Collaborators and Funding

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