Endocrine-disrupting Contaminants

Organization versus Activation

Organization vs. Activation

- Organizational effects
  - Permanent
    - Structural changes in tissues or organs
  - Occur early in life
  - Occur during critical or sensitive developmental periods
- Activational effects
  - non-permanent effects caused by the presence of a hormone
  - Transitory actions occurring during adulthood

Guillette LJ Jr, D.A. Crain, A.A. Rooney, D.B. Pickford. 1995. *Environ. Health Perspec.* 103(sup 7): 157-164.

Endocrine-disrupting Contaminants (EDCs)

- Mimic naturally occurring steroid
- Hormone receptor agonist or antagonists
- Alter enzymes responsible for hormone synthesis and degradation

EDCs
Organization vs. Activation

Organization

- Hormone mimicking EDCs in embryo or juvenile
- Removal of EDC contaminant permanent physiological, endocrine, developmental changes

Activation

- Hormone mimicking EDCs in adults
- Removal of EDC contaminant causes individual to return normal

What is Aroclor 1254?

- A commercial Polychlorinated biphenyls (PCBs) mixture with a 54 wt% of chlorine.
- PCBs were used in coolants, flame retardants, insulating fluids for transformers
- PCBs found to have effects on reproduction
  - Decreased hatching success
  - Low survival rates
  - Impaired development of eggs and embryos
  - Inhibition of spermatogenesis

Orn S., Andersson PL., Forlin L., Tysklind M., Norrgren L. (1998). *Arch Environ Contam Toxicol.* 35:52-57.

Coimbra A.M and M.A. Reis-Henriques. 2007. Tilapia larvae aroclor 1254 exposure: Effects on gonads and circulating thyroid hormones during adulthood. *Bull Environ Contam Toxicol.* 79:488-493.

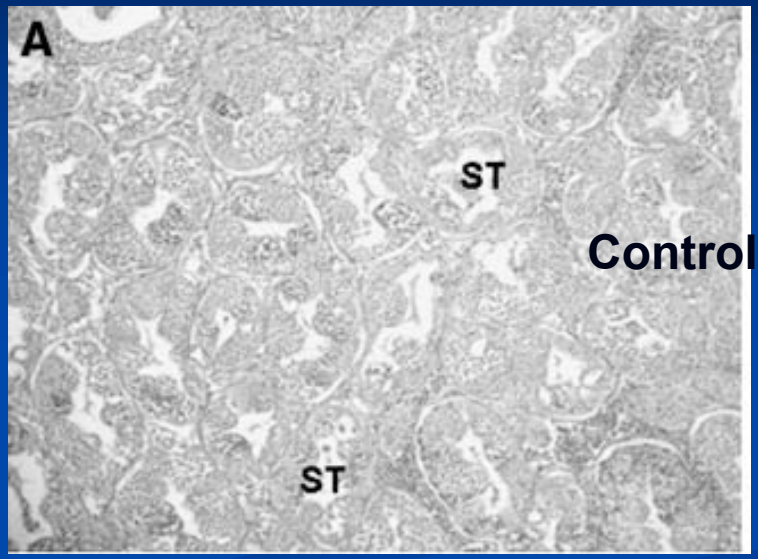
Aroclor 1254 – Organizational or Activational EDC?

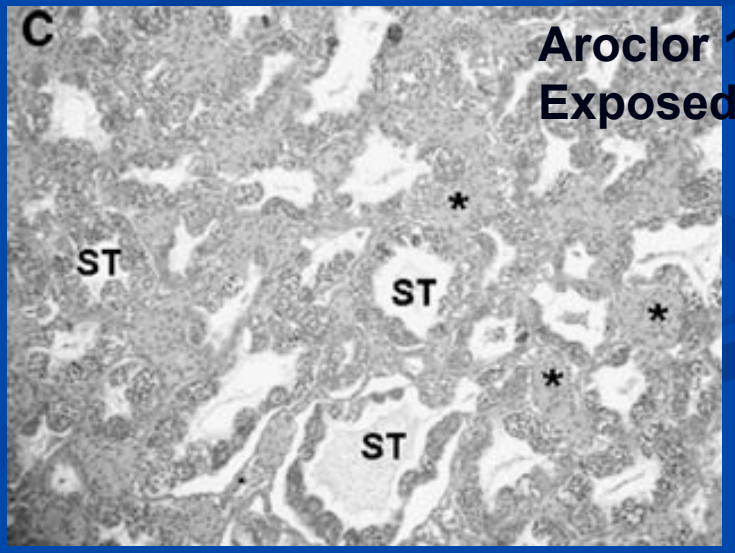
Methods:

- Fed 10 days post-hatch larvae (n=130/group) a commercial feed diet of Aroclor 1254-ethanol solution or only ethanol
- Aroclor 1254 fed larvae on diet for 40 days, placed on aroclor 1254-free diet for 18 months
- After 18 months, animals were sacrificed
  - Ovaries and testis observed
  - Plasma T_3 and T_4 measured

Aroclor 1254 Exposed Males

- Showed full urinary bladder
- Leydig cell hyperplasia
- Decreased germinal epithelium layer
- Decrease in plasma T_3 and T_4 concentrations





Coimbra & Reis-Henriques. 2007. *Bull Environ Contam Toxicol*. 79:488-493

Aroclor 1254 Exposed Females

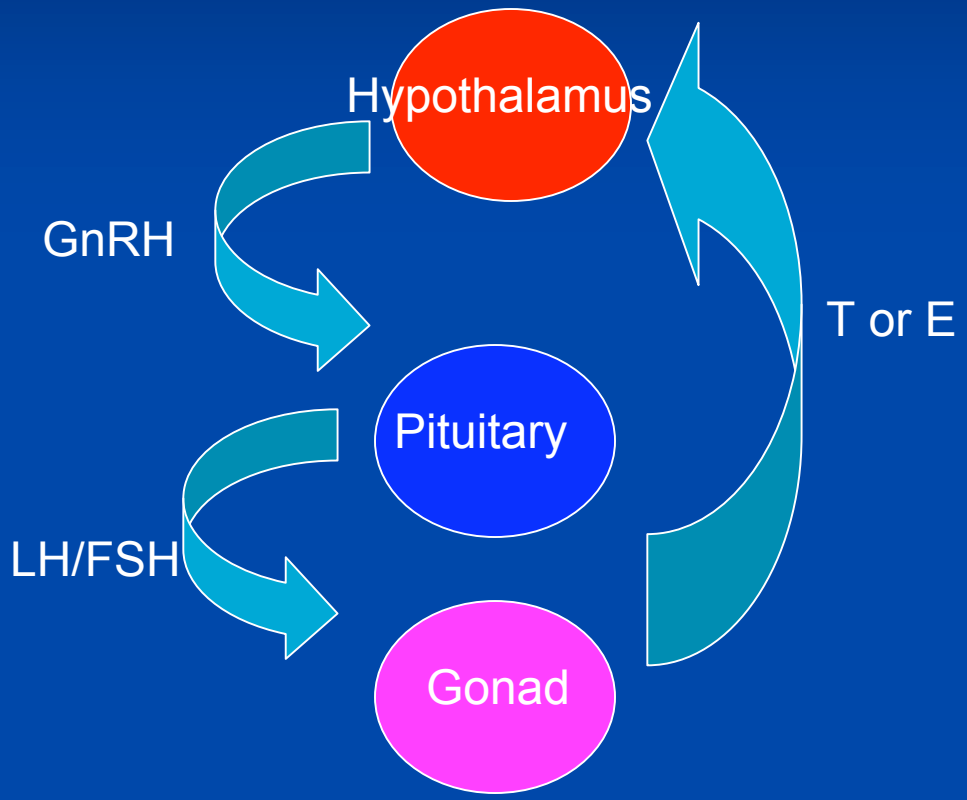
- Ovary lesions
- Atretic oocytes
- Average increase gonad somatic index
- Decrease in plasma T_3 and T_4 concentrations

Control Female

Aroclor 1254 Exposed Female

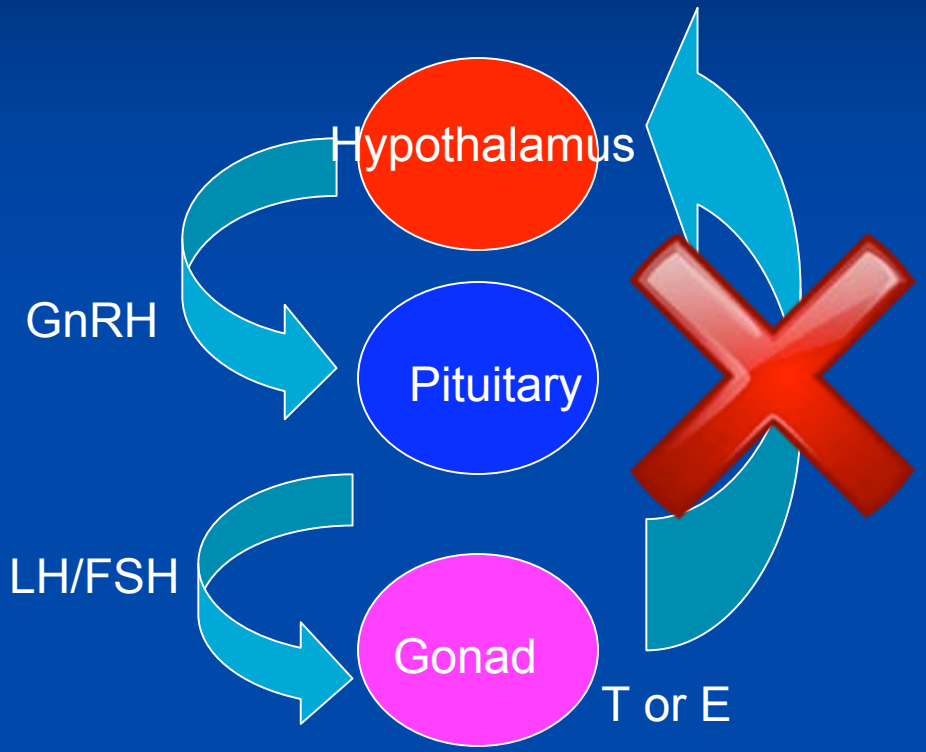
Coimbra & Reis-Henriques. 2007. *Bull Environ Contam Toxicol*. 79:488-493

Normal Negative Feedback in HPG Axis



- Increased T or E levels will feedback on Hypo and inhibit HPG axis
- Same feedback mechanism with thyroid stimulation and circulating T_3 and T_4 concentrations

EDCs Effect on Negative Feedback



- Disruption of HPG axis
- Leydig cell hyperplasia - stimulation of androgen, altered HPG axis
- Atretic oocyte – low LH, altered HPG axis, High P or low E
- Low T_3 and T_4 concentrations – hyper-stimulation of thyroid

Aroclor 1254: An Organizational EDC

- Removal of EDC permanently disrupted HPG axis in adult tilapia
- If EDC had an activational effect on HPG axis, then adult tilapia would have been fine (in theory)
- Therefore, exposure effects to low levels of PCBs, even for short periods of time, could permanently alter endocrine function