Endocrine Disrupting Contaminants

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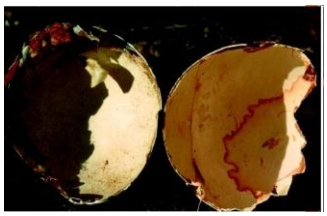
Introduction to Endocrine Disrupting Contaminants (EDC's)

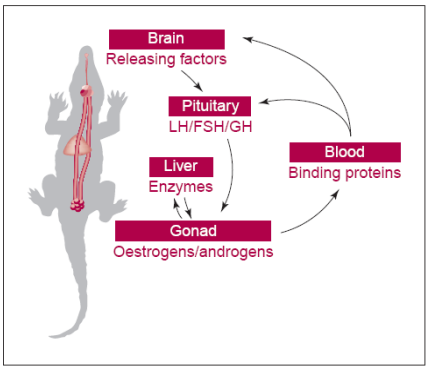
- Effects:
  1. Act as hormone receptor agonist or antagonist
  2. **Alter hormone production and endocrine source**
  3. Alter release of stimulatory or inhibitory hormones from pituitary or hypothalamus
  4. **Alter hepatic enzymatic biotransformations**
  5. Alter the concentration or functioning of serum binding proteins→ altering free hormone concentrations in serum

Background to Research

- Past research has shown pesticides, sewage, and pulp mill effluent disrupts endocrine function in wildlife populations.



EDC's



Focus of Research

•EDC's alter endocrine function in developing embryos, resulting in agonistic and antagonistic hormonal activity influencing sex determination in a wide range of species.

How EDC's alter sex determination

- Steroid hormones are important for sexual development in mammals as well as non mammalian vertebrates
- Found pharmaceuticals, anti-oestrogens block oestrogens ability to form ovaries, same goes for anti-androgens and testes

Normal Function

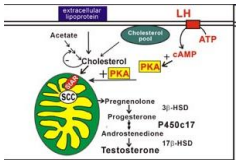
- Testosterone → Testes Formation
- Test. + Aromatase = Estrogen → Ovary Formation

EDC Function

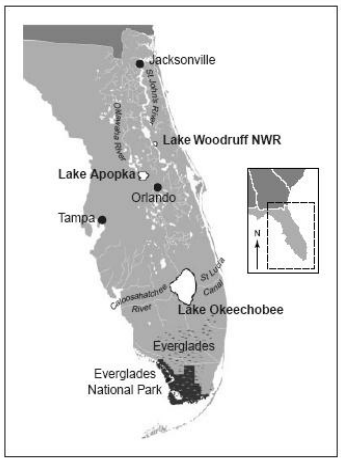
- Anti-oestrogens = acts as Aromatase antagonist, increasing Test.
- Anti-androgens = acts as Aromatase agonist, decreasing Test.

Pesticides, EDC's

- A metabolite of well known DDT, DDE, has exhibited oestrogenic activity (resulting in increased females) depending on species
- Not uncommon, found bioaccumulated EDC's in high concentrations in reptile eggs to cause sex reversals
  - EDC's caused block of STAR (steroidogenic acute regulatory protein) in Leydig cells, decreasing Test. Production



DDE PESTICIDE SPILL



- Contamination at Lake Apopka caused Male alligators to have decreased testosterone compared to Males from Lake Woodruff (3X)
- Females from Lake Apopka showed increased oestradiol levels compared to Lake Woodruff (2x)
- Juvenile alligators from Lake Apopka were transferred to Lake Okeechobee (no history of spills) after the spill and found to have abnormal hormone levels for many years

Juvenile Alligator Hormone Levels

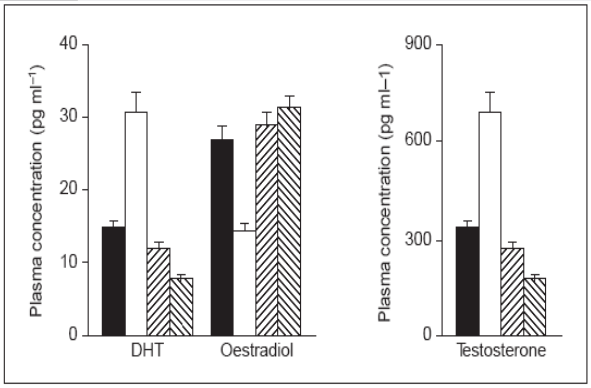


Fig. 3. Juvenile alligators (*Alligator mississippiensis*) from Lake Apopka, a lake contaminated with pesticides, pesticide metabolites and nutrients, exhibit altered plasma sex steroid concentrations compared with animals from a reference lake, Lake Woodruff. (■) Males from Lake Apopka; (□) males from Lake Woodruff; (▨) females from Lake Apopka; (▧) females from Lake Woodruff. Males have significantly lower plasma testosterone and DHT concentrations and higher plasma oestradiol concentrations than reference males. Females exhibit high plasma DHT concentrations compared with reference females. (Data from Guillette *et al.*, 1999b, Pickford *et al.*, 2000.)

- DHT Levels: Males from contaminated lake Apopka much lower DHT levels than reference lake, females with higher levels in Apopka.
- Males in contaminated Apopka had increased oestradiol, females oestradiol levels found to be pretty similar.
- Testosterone level patterns found to mimic DHT levels
- Appears 5 alpha reductase conversion of testosterone to DHT was unaffected by EDC's from this study

Alterations in hepatic biotransformations

- Normal role of liver:
  - Maintain homeostasis in all vertebrates
  - Maintain hormone homeostasis, allowing metabolizes peptide and steroid hormones
  - Production of distinct sexually dimorphic enzymes to regulate different enzymes

•EDC's

•Xenobiotics alter plasma testosterone concentrations, linked to:

•Altered hydroxylase enzyme activity in the liver

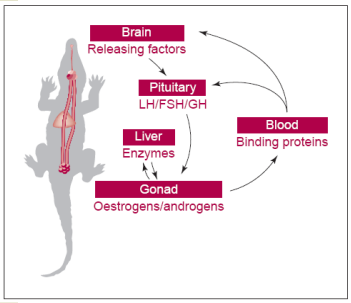
•Altered synthesis in the gonads

Alterations in hepatic biotransformations

- Possible mechanisms by which EDC's block biotranformations
  - Xenobiotics initiate the blocking of P-450 enzymes critical to the natural balance of circulating hormones
  - Oxidoreduction of testosterone to DHT and androstanediols can also become blocked by EDC's

Additional Thoughts: Sexual Dimorphism

- Essentially the idea that there are different hormone titers for both males and females



•It has been proposed that there is a link between GH, Sex hormones, and liver activity

•Hypothalamo-pituitary-hepatic axis controls liver activity in a sexually dimorphic manner, allowing EDC's to disrupt in a dimorphic manner

•Increased testosterone levels and liver enzymatic activity associated with increased testosterone could, for example, communicate to the the pituitary to release more or less GH and produce a larger or smaller effect.

•**You can see how there is the potential for EDC's to contaminate and disrupt many processes at many different sites!**

EDC Detection

- EDC's are detected through direct presence in plasma, however, not always present in detectable concentrations
- Many times hormonal imbalances serve as the indicator that EDC's are present, exactly which EDC may not always be detectable
- Detection via cross reactivity by use of antibodies allows known contaminant detection
- Compilation of data from many sources may be important to create legislation against allowing certain contaminants to damage wildlife populations

Conclusions

- EDC's potentially alter development of the reproductive system and liver
- More research is needed to examine effects of EDC's on binding proteins
- EDC's serve as a definitive mechanism by which embryos are altered
- Because EDC's affect multiple systems, coupled with complex mix of chemicals, indicate great amounts of research are needed to understand the long term implications of endocrine disruption for populations of wildlife species

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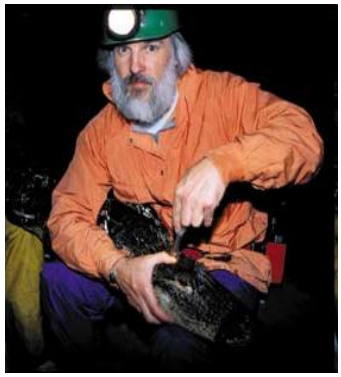

Lou gathering a blood sample from a juvenile alligator to test for environmental contaminants at Lake Apopka, Florida.