

Special Topic: Endocrine Disruption

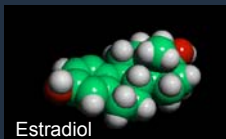
Principles of Environmental Toxicology
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University of Idaho

Learning Objectives

- Understand the scientific basis of environmental endocrine disruption.
- Explore the endocrine disruption hypothesis.
- Review the classic case studies that have increased awareness in the public about environmental endocrine disruption.
- Understand recent research and policy issues related to environmental endocrine disruption.
- Explore the future pathways of analysis in the study of endocrine disruption.

Endocrine Disrupters

- Chemicals which interfere with endocrine system function.
- Endocrine system consists of glands and the hormones they produce.
 - Pituitary, thyroid, and adrenal glands, the female ovaries and male testes.



Endocrine Disrupters

- Hormones are biochemicals.
 - Produced by endocrine glands.
 - Travel through the bloodstream and cause responses in other parts of the body.
- Hormones of primary concern.
 - Estrogen, androgen and thyroid hormones.



Video

- "Fooling with Nature", PBS Frontline

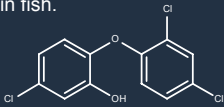
Endocrine Disruption Observations

- Cryptorchidism in the Florida panther.
- Small baculum in young male otters.
- Small penises in alligators.
- Sex reversal in fish.
- Altered social behavior in birds.
- Proposed that EDCs also may have contributed to increases in testicular cancer and hypospadias and the reported decline in human sperm counts.



Example: Antibiotic Soap

- Triclosan, the common antiseptic, was found in 57.6% of the United States water resources surveyed (USGS).
- A broad-spectrum antibacterial - antimicrobial agent classified as a Class III drug by the FDA.
- Bacteriostatic activity against a wide range of bacteria has lead to popular use in:
 - Personal care products, cosmetics, anti- microbial creams, acne treatment, lotions and hand soaps, plastics, polymers and textiles.
- Linked to estrogenic effects in fish.



Male-to-Female Sex Reversal

- Fish: “complete, permanent, and functional male-to-female sex reversal in the Japanese medaka (*Oryzias latipes*, d-rR strain) after a onetime embryonic exposure to the xenoestrogen *o*,-DDT”

Edmunds, JSG, RA McCarthy and JS Ramsdell.
2000. Permanent and Functional Male-to-Female
Sex Reversal in d-rR Strain Medaka (*Oryzias latipes*)
Following Egg Microinjection of *o*,-DDT.
Environmental Health Perspectives 108:219-224



Hermaphroditism - Demasculinization

- Frogs: “Atrazine (0.1 ppb) induced hermaphroditism and demasculinized the larynges of exposed males (1.0 ppb). Male (African clawed frogs) suffered a 10-fold decrease in testosterone levels when exposed to 25 ppb atrazine.

Hayes, TB, A Collins, M Lee, M Mendoza, N Noriega,
AA Stuart, and A Vonk. 2002. Hermaphroditic,
demasculinized frogs after exposure to the herbicide,
atrazine, at low ecologically relevant doses.
Proceedings of the National Academy of Sciences
(US) 99:5476-5480.



Male-to-Female Sex Reversal

- Salmon: “a high incidence (84%) of a genetic marker for the Y chromosome in phenotypic females sampled from the wild... It appears likely that female salmon with a male genotype have been sex reversed, creating the potential for an abnormal YY genotype in the wild that would produce all-male offspring and alter sex ratios significantly.”

High Incidence of a Male-Specific Genetic Marker in
Phenotypic Female Chinook Salmon from the Columbia
River. Nagler, JJ, Bouma, J, Thorgaard, GH, Dauble, DD
Environmental Health Perspectives. Vol. 109, no. 1,
pp. 67-69. Jan 2001



Sex Ratio, Hermaphroditism Reproductive Failure

- Oysters: “nonylphenol has been found to induce long-term and transgenerational effects in the Pacific oyster ...when larvae are exposed to environmentally relevant concentrations of nonylphenol ...change in the sex ratio ...increase in the incidence of hermaphroditism (up to 30%) ... (next generation) gamete viability, up to 100% mortality.”

Nice, HE, D Morritt, M Crane and M Thorndyke.
2003. Long-term and transgenerational effects
of nonylphenol exposure at a key stage in the
development of *Crassostrea gigas*.
Possible endocrine disruption?
Marine Ecology Progress Series 256:293-300.

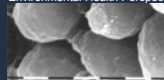


Additive Effects of Weak Xeno-estrogens

- Yeast estrogen screen: “when combined with estradiol... bisphenol A or *o*,*p*’-DDT contribute to... additive combination effects between xenoestrogens and steroidal estrogens.”
- The combined additive effect of the 11 xenoestrogens led to a dramatic enhancement of the hormone's action, even when each single agent was present below its NOEC.”

Rajapakse, N, D Ong and A Kortenkamp. 2001. Defining the
Impact of Weakly Estrogenic Chemicals in the Action of
Steroidal Estrogens. Toxicological Sciences 60: 296-304.

Rajapakse, N, E Silva and A Kortenkamp. 2002.
Combining Xenoestrogens at Levels below
Individual No-Observed-Effect Concentrations
Dramatically Enhances Steroid Hormone Action.
Environmental Health Perspectives 110:917-921



Anti-Estrogenic Polycyclic Musks

• "The polycyclic musks (AHTN) and (HHCB) are used as fragrance ingredients in perfumes, soaps, and household cleaning products....are known to be ubiquitously present in the aquatic environment, and because of their lipophilic nature, they tend to bioaccumulate in aquatic biota... musks bioaccumulated in the fish, with concentrations... which were roughly 600 times higher than doses... are shown to be *antiestrogenic* in an *in vivo* fish assay that focuses solely on ER-mediated effects."

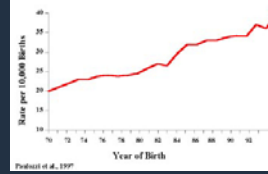
In Vitro and in Vivo Antiestrogenic Effects of Polycyclic Musks in Zebrafish Richard H. M. M. Schreurs*, Juliette Legler, Elsa Artola-Garicano, Theo L. Strating, Peter H. Lanser, Willem Seinen, and Bart van der Burg.
Environ. Sci. Technol., 38 (4), 997-1002, 2004.



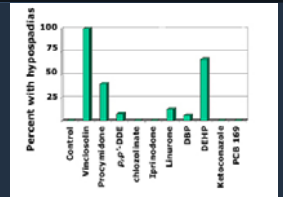
Hypospadias

Incomplete Masculinization of the Reproductive Tract

HYPOSPADIAS in the US



Paulozzi et al., 1997



Paulozzi LJ, Erickson JD, Jackson RJ. 1997. Hypospadias trends in two U.S. surveillance systems. *Pediatrics* 100:831-834.

Paulozzi LJ. 1999. International trends in rates of hypospadias and cryptorchidism. *Environmental Health Perspectives* 107:287-302.

Gray LE, C Wolf, C Lambright, P Mann, M Price, RL Cooper and J Ostby. 1999. Administration of potentially antiandrogenic pesticides (procymidone, linuron, iprodione, chlorzoxinone, p,p'-DDE, and ketoconazole) and toxic substances (dibutyl- and diethylhexyl phthalate, PCB 169, and ethane dimethane sulphonate) during sexual differentiation produces diverse profiles of reproductive malformations in the male rat. *Toxicology and Industrial Health*. 15:94-118.