Endocrine Disruptors

Perspective of the Endocrine Society

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The Endocrine Society

- Founded in 1916
- >15,000 members worldwide
  - Basic and clinical scientists
  - Physicians in practice
  - Students, nurses, administrators, educators
- With other Societies of Endocrinology, they represent the world's leading experts on hormones and the endocrine effects of environmental chemicals

The Endocrine Society

- Endocrine Disrupting Chemicals represent a special class of toxic substance
- As a result, principles of endocrinology must guide the design and interpretation studies used in the risk assessment process.
- Current “validated” guideline studies are not adequate and weight-of-evidence guidance documents weaken the ability of these studies to limit risks of human and wildlife exposure.

THE ENDOCRINE SOCIETY®

The Endocrine System

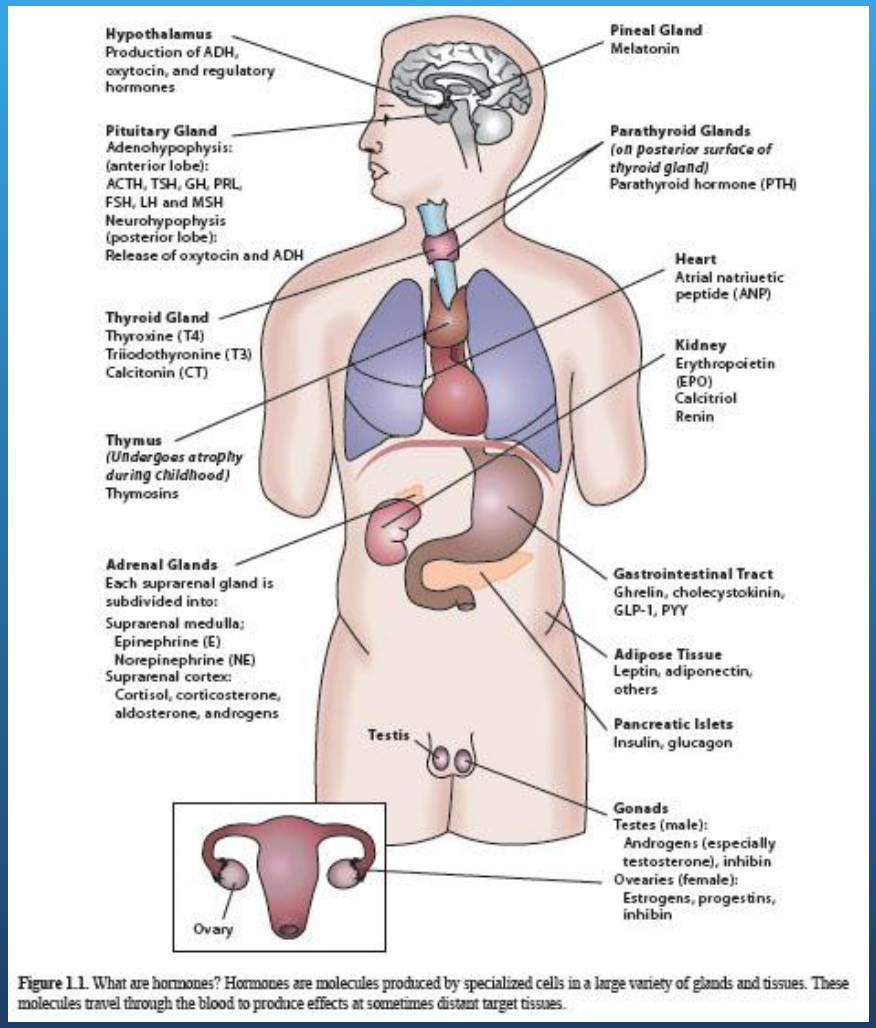

Figure 1.1. What are hormones? Hormones are molecules produced by specialized cells in a large variety of glands and tissues. These molecules travel through the blood to produce effects at sometimes distant target tissues.

- Endocrine systems are complex, with over a hundred different molecules that are active throughout our lifespan, from the early stages of fetal development to maintaining the functioning of our bodies until death.
- EDCs are already known to interfere with E, A, T, Adrenal hormones, Insulin, many others.

Definition of an EDC

- An ED is an exogenous agent that interferes with the production, release, transport, metabolism, binding, action or elimination of natural hormones in the body responsible for the maintenance of homeostasis and the regulation of developmental processes. –US EPA, 1996
- An ED is an exogenous chemical, or mixture of chemicals, that interferes with any aspect of hormone action. – The Endocrine Society, 2012

Definition of an EDC

- EXAMPLE:
  - A change in blood level of hormone represents “disruption” only if the result is that hormone is not delivered (or is delivered inappropriately) to the target tissue and receptor (i.e., interferes with hormone action)
- NORMAL ENDOCRINE FUNCTION: CHOCOLATE BAR
- Chocolate bar increases blood level of glucose
- Increase in glucose causes insulin to be released
- Insulin causes tissues to take up glucose (this is NOT “homeostasis”)
- Thus, a chocolate bar is not an EDC

Definition of an EDC

- EXAMPLE OF AN EDC: CHOCOLATE BAR
  - In contrast, an EDC would be an exogenous chemical, or mixture of chemicals, that interferes with:
    - The ability of glucose to cause insulin release
    - The ability of insulin to interact with its receptor
    - The ability of insulin-receptor interaction to cause glucose uptake and/or utilization

Definition of an EDC

- LIKEWISE: An EDC is an exogenous chemical, or mixture of chemicals, that:
  - Interferes with thyroid hormone action during brain development and reduces the intellectual potential of the individual and population
  - Interferes with fat development, predisposing the individual and population to obesity and diabetes
  - ETC!

Principles of Endocrinology

- Hormones have very specific effects because they act via receptors. Hormone receptor expression depends on:
  - Stage of the life cycle
  - Tissue/cell
- Many hormone systems include multiple receptor types.
- EDCs interact in ways that are not predictable (so far)
  - Receptor type
  - Cell type
  - Stage of the life cycle
  - etc

Current Validated Test Systems

- Largely fail to evaluate hormone action (e.g., thyroid)
- Fail to focus on appropriate end-points of hormone action
- Fail to account for “mosaic” effects of EDCs on hormone action.
- Designed in the 30’s and 40’s, largely fail to be predictive of EDC effects on human health TODAY

Current Validated Test Systems

- EXAMPLE: POLYCHLORINATED BIPHENYLS (PCBs)
  - PCB production was banned in the US by Congress in the 1970's (persistence and suspected carcinogen)
  - Research since then demonstrate that PCBs cause a number of adverse outcomes in the human population
  - Mechanistic research has shown that these adverse effects are due in part to PCB effects on thyroid hormone action.
- HOWEVER: EPA's EDSP WOULD STILL FAIL TO IDENTIFY PCBs AS ANTI-THYROID EDCs.
- What else are we missing?

Inaction Sacrifices Human Potential and Costs Money

ABSTRACT **A 2002 analysis documented $54.9 billion in annual costs of environmentally mediated diseases in US children. However, few important changes in federal policy have been implemented to prevent exposures to toxic chemicals. We therefore updated and expanded the previous analysis and found that the costs of lead poisoning, prenatal methylmercury exposure, childhood cancer, asthma, intellectual disability, autism, and attention deficit hyperactivity disorder were $76.6 billion in 2008. To prevent further increases in these costs, efforts are needed to institute premarket testing of new chemicals; conduct toxicity testing on chemicals already in use; reduce lead-based paint hazards; and curb mercury emissions from coal-fired power plants.**

Trasande & Liu, 2011. Health Affairs 30(5):863-870.

Principles of Endocrinology

- EDCs represent a special class of environmental toxic agent.
- EDCs ultimately affect hormone receptors
- Hormone receptors are very selectively expressed during development.
- Interfering with hormone action during development can be assumed to have an adverse outcome at the population level.