



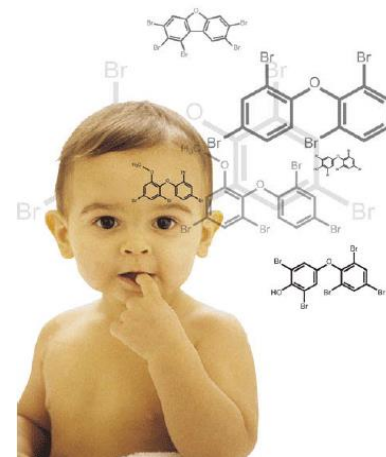
National Institute of Environmental Health Sciences
Your Environment. Your Health.

Overview of Endocrine Disruptor Action: Should We Be Concerned ?

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We all Carry a Chemical Body Burden

- 287 chemicals in
- 47 chemi
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-
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- PF
- PBDE
- Triclosan in
- PCBs in 100%

The presence of chemicals in the womb does not mean that they are causing harm.

However, it does mean that we have accepted a strategy whereby every pregnant woman is contaminated with hundreds of man made chemicals ...without her consent....with the potential to cause harm.



Endocrine Disruptor Definition

An Endocrine Disruptor is an exogenous chemical, or mixture of chemicals, that interferes with any aspect of hormone action.

*Zoeller et al, Endocrine Society Position Statement,
Endocrinology 153: 4097–4110, 2012*



Endocrine Disrupting Chemicals

HERBICIDES

Pesticides

- Alachlor
- Amitro
- Atrazine

Herbicides

- Trifluralin

Fungicides

- Fenarimol
- Hexachlorobenzene

Solvents

- Tri-butyl-tin
- Vinclozolin
- Zineb

METALS

INSECTICIDES

Flame Retardants

- Carbaryl
- Chlordane
- Chlordecone

Industrial byproducts

- DDT and metabolites
- Endosulfan

Surface protectors

- Methomyl
- Methoxychlor

Sunscreens

- Transnonachlor
- Toxaphene

Testosterone synthesis inhibitor *Estrogen receptor agonist*
Thyroid hormone disruptor *Androgen receptor antagonist*

INDUSTRIAL CHEMICALS

Plastics

- Bi
- Pol
- Butylhydroxyanisole
- Cadmium
- Chloro- & Bromo-diphenyl

Plasticizers

- Di
- Fu
- Lead
- Manganese
- Methyl mercury

Cosmetics

- Non
- Oc
- PBB
- PCBs
- Pentachlorophenol

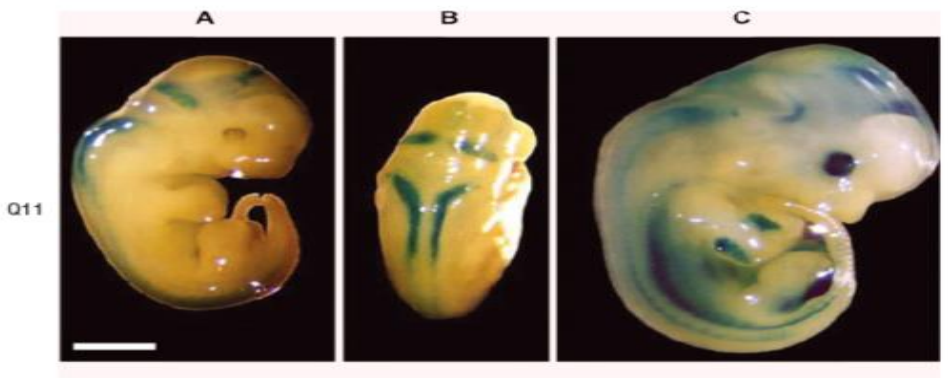
Over 900 EDCs

- p-tert-Pentylphenol
- Phthalates
- Styrene

Principles of Endocrine Disruptor Action

- Many EDCs act via Receptors:
 - EDC response depends on concentration, receptor affinity and co-regulatory proteins.
 - EDC responses are **tissue specific**.
 - Receptor cross talk at high doses.
- EDCs can act at Low Doses throughout the lifespan.
- EDCs can show Non-Monotonic Dose-Response Curves.
- EDC effects are Life-Stage Specific

EDC Action is Life-stage Specific



Developmental Effects (Organizational)

- Most sensitive exposure window
- Stage and tissue specific
- Lack of feedback mechanisms
- Incomplete differentiation
- **A bad start...lasts a lifetime!**
- Functional changes leading to persistent and latent effects
- Increased disease risk later in life

Adult Effects

(Activational)

- Usually higher doses
- Effects as long as EDC present
- Can augment developmental effects



Why is Development a Sensitive Window?



Epigenetics

- Epigenetics provides cells the capability to sense, interpret, and act upon environmental stimuli by modifying gene expression.
- Epigenetics provides plasticity that allows adaptation during times of early environmental stressors such as prenatal nutrition, stress and environmental chemical exposures...many positive adaptive effects.
- Epigenetic changes can be persistent across cell divisions and generations but are also dynamic across a lifetime.

Disease Risk Increased by Developmental Exposures to EDCS (Human)

Reproductive/Endocrine

- Breast/prostate cancer (BPA)
- Endometriosis (Dioxin, PCBs)
- Infertility (Phthalates, Estrogens, Pesticides)
- Diabetes/metabolic syndrome (BPA)
- **Early Puberty** (Estrogens, BPA)
- **Obesity** (BPA, Tributyl Tin, Organochlorine Pesticides)

Immune/Autoimmune

- **Susceptibility to infections** (Dioxin, Perfluorinated compounds, Arsenic)
- Autoimmune Disease (Dioxin)

Pulmonary/Cardiovascular

- **Asthma** (Air Pollution)
- Heart disease/hypertension (BPA)
- Stroke (PCBs)

Brain/Nervous System

- Alzheimer's disease (Lead)
- Parkinson's disease (Pesticides)
- **ADHD/learning disabilities** (PCBs, Lead, Ethanol, Organochlorine, Pesticides)

EDCs: Should We Be Concerned?

- The high incidence and the increasing trends of many endocrine-related disorders in humans;
- Observations of endocrine-related effects in wildlife populations;
- The identification of many endocrine-disrupting chemicals in the environment and in humans;
- Increased body burden of EDCs in humans and wildlife;
- Increased body burden of EDCs across the globe;
- Lack of knowledge of sources of EDCs;
- Inadequate testing.

There are no longer any pristine areas in the world devoid of environmental contamination!

Implications of Principles of Endocrinology for EDC Toxicity Testing and Human Health

- High dose effects are likely to be nonspecific.
- Need wide dose responses covering “low dose” concentrations.
- High dose effects don’t predict low dose effects.
- Can’t extrapolate from high dose studies to what will happen at lower untested doses.
- Must test developmental exposures and assess effects across lifespan.
- Must test mixtures.
- Need improved testing protocols to take account these characteristics of EDCs.

The Good News....

Focus on:

- **Prevention of Disease**
 - Focus on pregnancy, early childhood and puberty as sensitive periods
 - Reduced exposures to environmental agents during development
- **Development of biomarkers to indicate developmental exposures**
- **Improved toxicity testing**
- **Green chemistry...improved next generation chemicals**

Not the End... but the end of the beginning

Bemidji Statement:

“We have the sacred right and obligation to ensure that our decision-making is guided by consideration of the welfare and well being of the seventh generation to come.”

Thank you...