INTRODUCTION TO ENDOCRINE DISRUPTING CHEMICALS (EDCs)

A GUIDE FOR PUBLIC INTEREST ORGANIZATIONS AND POLICY-MAKERS

Part 2 – EDCs – The Science

CHE-Alaska Webinar
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Background and History

Founded in 1916, the **Endocrine Society** is the world's oldest, largest, and most active organization devoted to research on hormones and the clinical practice of endocrinology. The Endocrine Society's membership consists of over 18,000 scientists, physicians, educators, nurses, and students in more than 100 countries. Society members represent all basic, applied and clinical interests in endocrinology. Included among the Society's members are the world's leading experts on the health effects of EDCs.

Background and History

2005: Endocrine Society - Forum on EDCs, ENDO 2005 (San Francisco, CA)

2009: Endocrine Society - 2nd Forum on EDCs, ENDO 2009 (Washington, DC)

Endocrine Reviews, June 2009, 30(4):293–342

Endocrine-Disrupting Chemicals: An Endocrine Society Scientific Statement

Evanthia Diamanti-Kandarakis, Jean-Pierre Bourguignon, Linda C. Giudice, Russ Hauser, Gail S. Prins, Ana M. Soto, R. Thomas Zoeller, and Andrea C. Gore

AMA, American Public Health Association, WHO and U.N. Environment Programme, ACOG, ASRM, British Royal College of Obstetrics & Gynaecology

Scientific Writing Group

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Definition of an EDC

Endocrine-Disrupting Chemicals and Public Health Protection: A Statement of Principles from The Endocrine Society

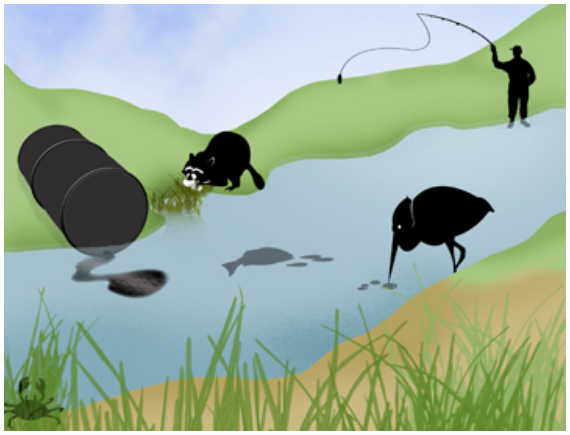
R. Thomas Zoeller, T. R. Brown, L. L. Doan, A. C. Gore, N. E. Skakkebaek, A. M. Soto, T. J. Woodruff, and F. S. Vom Saal

Endocrinology, September 2012, 153(9):4097–4110

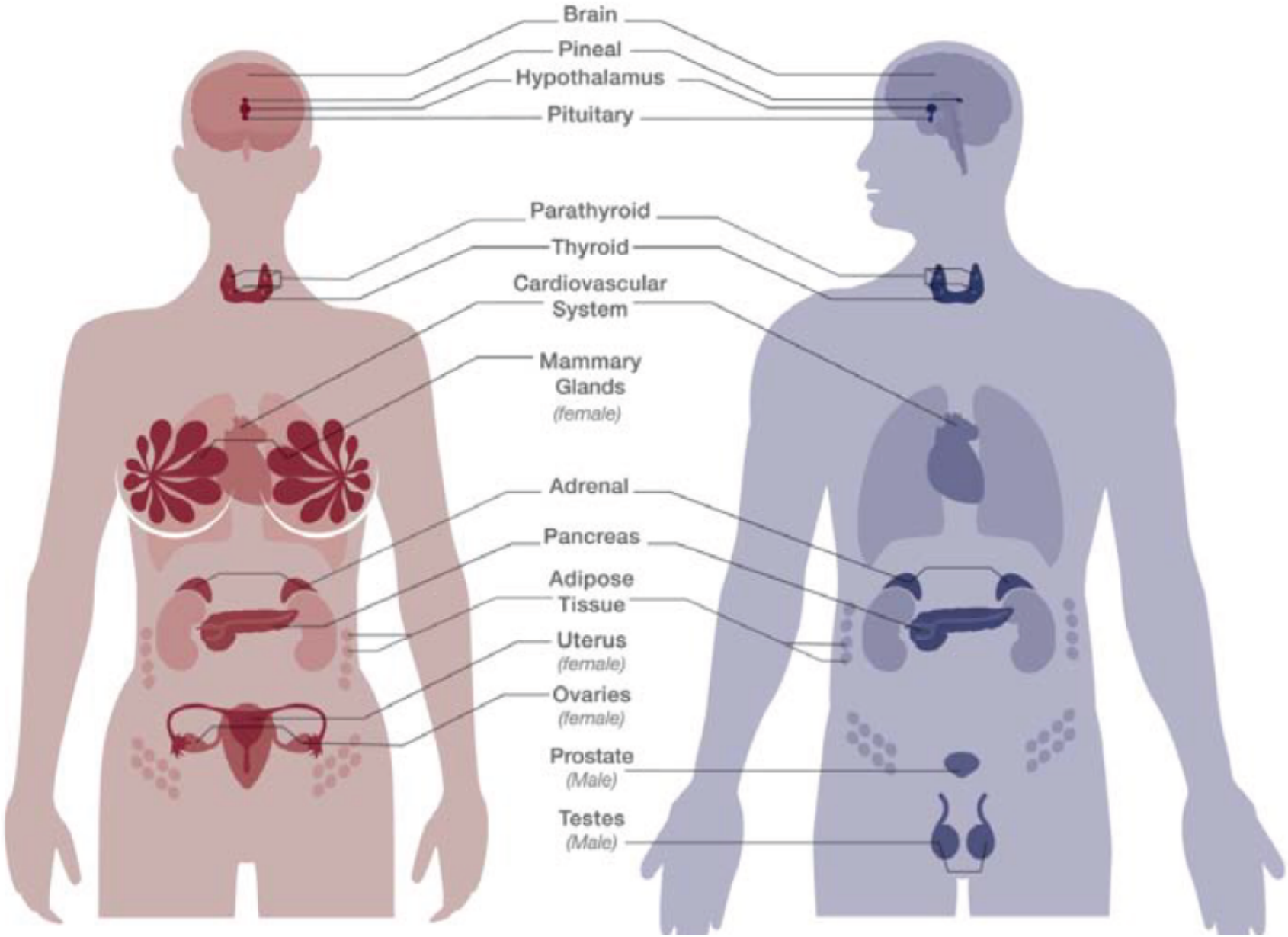
"An endocrine disruptor is an exogenous chemical, or mixture of chemicals, that interferes with any aspect of hormone action."

Exposures to EDCs

- Household chemicals
- Food, especially processed food
- Plastics
- Personal care products
- Air, water
- Pesticides



Hormones and Endocrine Systems



Key Principles

- Endocrine systems are essential for development, reproduction, and health.
- EDCs can mimic or block actions of natural hormones, and interfere with their production, release, and metabolism.
- As the body's interface with the environment, endocrine systems are vulnerable to EDCs.
- Early life development is very sensitive to EDCs: "The timing [not just the dose] makes the poison."
- A single EDC class can act at many types of targets.
- Hormones – and EDCs – can interact to have complex health effects that may not be observed for years, or decades.

The special vulnerability of the fetus, infant, and child

BOX 1: THE DEVELOPMENTAL ORIGINS OF HEALTH AND DISEASE (DOHAD)

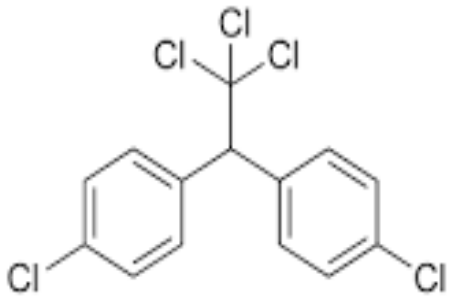
DOHaD, also referred to as the "Fetal basis of adult disease" (FeBAD), is based on scientific evidence that the roots of many diseases and dysfunctions occur very early in life, especially the embryo, fetus, infant, and child. For example, under- or over-nutrition of a pregnant woman has an influence on the fetus's propensity to develop metabolic disorders including obesity, diabetes, and others, later in life. This research has since been extended to environmental influences such as cigarette smoking, pollution, and environmental chemicals. Other evidence has shown that the developing germ cells – precursors to the sperm and egg cells of the fetus – are quite vulnerable to disruptions from even low doses of EDCs. More recently, the nervous system, the development of which begins in early gestation and continues well into childhood, has been found to be very sensitive to EDC exposures. Certain cancers, especially reproductive cancers, seem to have their origins in early life. While the manifestation of disease or disorder may not be apparent at birth, following a latent period the results of these exposures become evident, often in adolescence, adulthood or aging. Thus, DOHaD is a key concept in understanding the influence of EDC exposures during these vulnerable periods.

EDC Examples

- Pesticides (DDT, chlorpyrifos)
- Products (children's products – lead; electronics – brominated flame retardants)
- Food contact materials (BPA)

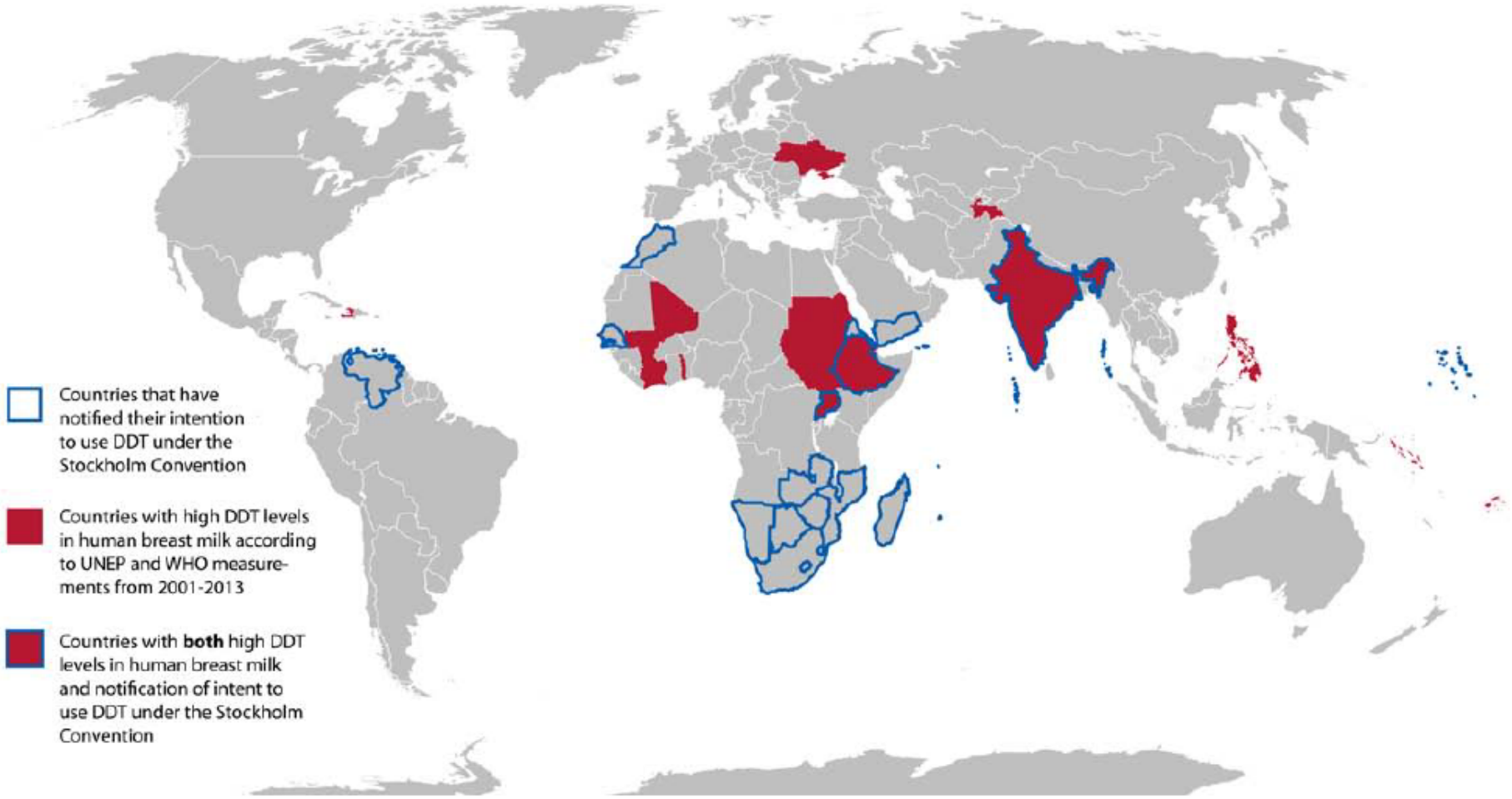
Pesticides - DDT

- What is it?
  - Organochlorine insecticide.
- Where is it used?
  - Used for disease vector control in accordance with WHO guidelines. May be used illegally in agriculture.
- Where are we exposed?
  - Majority through the food supply. Particularly problematic in children and the elderly.



DDT in Human Milk

FIGURE 2 LEVELS OF DDT IN HUMAN MILK



Data reflects survey results over the period 2001-2013 and current DDT registry information from the Stockholm Convention

Pesticides - DDT

- Science on why DDT is an EDC
  - DDTs modify numerous endocrine pathways: thyroid, estrogen, androgen, kidney and cardiovascular hormones, insulin, neuroendocrine.
  - Adverse outcomes due to exposure to the fetus and child are the most pronounced.

BOX 3: HUMAN HEALTH CONSEQUENCES OF EXPOSURE TO DDTS

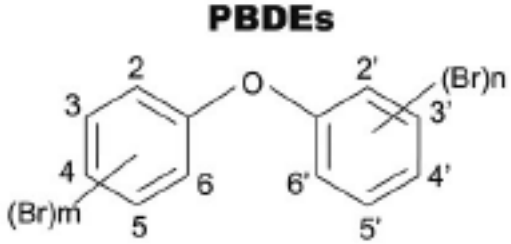
- Reduced fertility
- Urogenital birth defects (males)
- Impaired breast feeding
- Type 2 diabetes
- Cancer

Pesticides - DDT

- Negative health outcome: Type 2 diabetes (T2D)
  - Epidemiological studies demonstrate strong positive association between the DDT metabolite (DDE) and T2D risk.
  - Animal experiments show that low-prenatal and high-adulthood exposures cause T2D in rodents.
  - Blood glucose is increased, and mice become insulin resistant.

Products – Electronics – Brominated flame retardants (BFRs)

- What are they?
  - Polybrominated diphenyl ethers (PBDEs) are POPs.
- Where is it used?
  - Flame retardants in computers, electronics, textiles, furniture, building materials.
- Where are we exposed?
  - BFRs are released into the environment, get into air and dust, and may be ingested and inhaled.
  - Processing of waste
  - Occupational – firefighters, manufacturing, carpet installers.

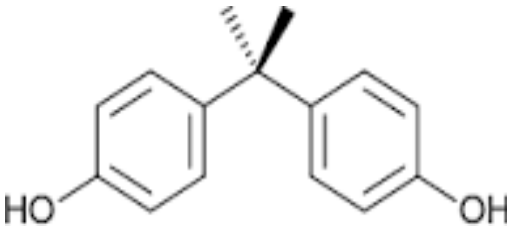


Products – Electronics – Brominated flame retardants (BFRs)

- Science on why BFRs are EDCs
  - BFRs and their breakdown products interfere with the thyroid system – act via thyroid receptors, or enzymes involved in metabolizing thyroid hormones.
  - Some BFRs can bind to estrogen receptors.
- Negative health outcome: Adverse neurodevelopment
  - Epidemiological studies show that PBDEs are associated with thyroid disruption, that in turn is associated with reduced IQ, concentration, fine motor coordination, and cognition.
  - Brain development is altered in animal studies.

Food Contact Materials – Bisphenol A

- What is it?
  - A synthesized molecule used in manufacture of plastics and food containers.
- Where is it used?
  - Hard plastics, liners of canned foods, thermal paper receipts, plastic water pipes.
- Where are we exposed?
  - Leaching from food and beverage containers, house dust, paper receipts.



Food Contact Materials – Bisphenol A

- Science on why BPA is an EDC
  - BPA was first synthesized as a potential estrogenic pharmaceutical.
  - Estrogens play critical roles in brain development, mammary gland, and male/female reproductive tracts.
  - Affects thyroid signaling and energy balance pathways.
- Negative health outcome: Behavior and reproductive health
  - Epidemiological data: Disorders of reproduction, behavior, energy balance, cardiovascular systems.
  - Ovarian functions (follicle development, ovulation) are perturbed.
  - Linked with endometriosis, PCOS, miscarriage, premature birth.
  - Animal studies: Neurobehavior, anxiety, aggression.

There is no such thing as a “safe dose”

- Natural hormones act at extremely low levels.
- Hormone receptors are exquisitely sensitive.
- There are periods of life when tissues may have no natural hormone exposure – so the presence of an EDC can trigger a biological response.
- EDCs that can act via hormone receptors can do so at extremely low levels – including those measured in human tissues.
- Safety testing does not take into account periods of developmental vulnerability.
- “Safe thresholds” cannot be determined by traditional testing.
- Testing rarely considers mixtures.

EDCs: The problem of cause-and-effect in humans

- Traditional toxicological testing is inadequate to identify EDCs.
- Developmental vulnerability and lag time to disease.
- Exposures to complex mixtures of chemicals throughout our lives.
- People have unique genomes and genetic predispositions.
- Influence of lifestyle.
- Cannot do a “controlled” experiment.

Why are endocrinologists confident that EDCs are an international public health problem?

- Twin studies show the key role of the environment in human diseases.
- High-dose and occupational exposure data.
- Experimental animal studies based on carefully controlled exposures with appropriate vehicles (placebos) and positive controls (e.g. estrogens).
- Laboratory cell line work identifying how putative EDCs act – e.g. cells that express estrogen receptors.
- Epidemiological data in humans linking higher body burdens of chemicals to increased disease prevalence.
- The Toxic Substances Control Act inventory of the U.S. EPA includes 85,000 chemicals, few of which are tested for health effects – and humans are exposed to many.