EDC Criteria and next steps: A scientific perspective

Barbara Demeneix, BSc, PhD, DSc
Chair, Endocrine Society EU Task Force

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Outline

- The Endocrine Society – Who we are and how we are involved
  - My research and background
- The Guidance Document for Implementing the EDC criteria – What does the science say and what are the gaps?
- **What Is Needed:**
  - A revised EU strategy for EDCs
  - Additional investment in research

The Endocrine Society

- Over 18,000 members from over 120 countries
- Basic researchers, clinical scientists, clinicians in practice
- We unite, lead, and grow the endocrine community to accelerate scientific breakthroughs and improve health worldwide
- Involved in EU EDC Criteria process since 2013

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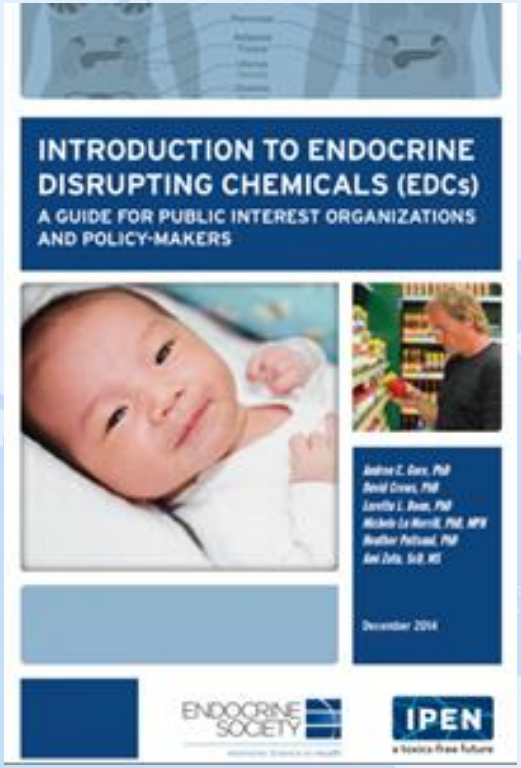
EDCs are not like other chemicals

- Low dose effects, no threshold
- Windows of vulnerability - fœtus & children
- Developmental origin of adult disease
- Mixtures: on average every baby born is exposed to over 100 potential EDCs



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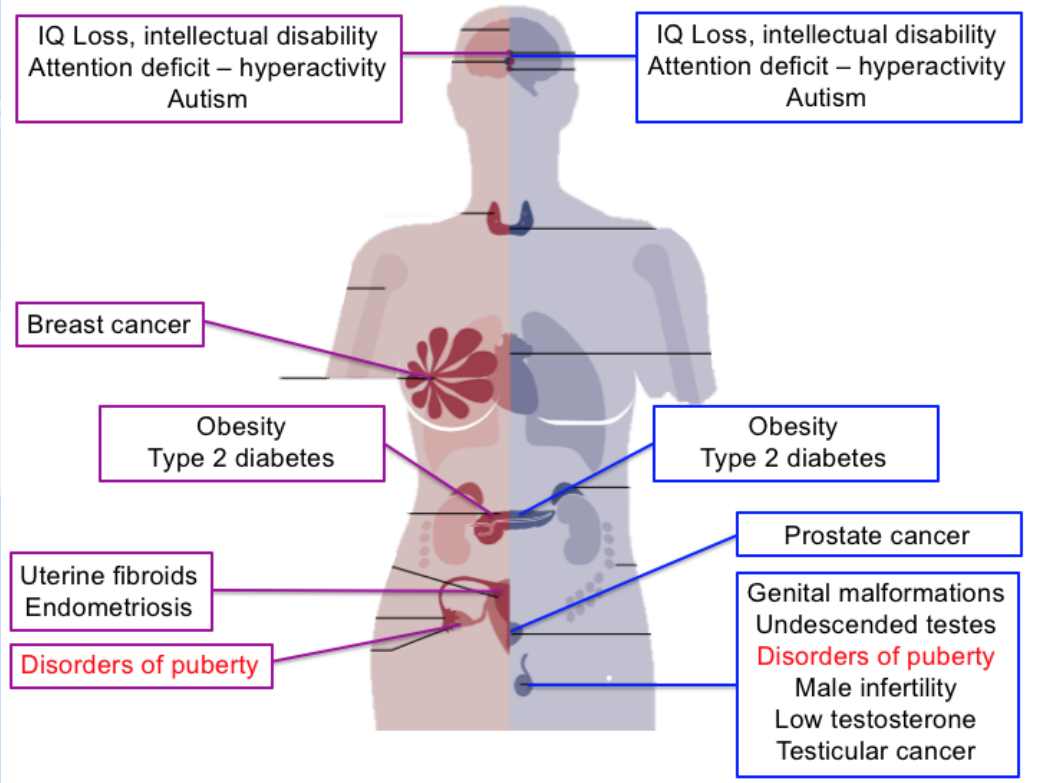
EDCs have been linked by epidemiology and experiment to multiple non-infectious diseases

- EDC Science has advanced rapidly in recent years
- www.endocrine.org/edc
- Better regulation needed to protect public health



My own focus: Thyroid EDCs & Brain Development

- Since 2001 - asked to represent France on OECD chemical testing committees
- Co-founded Watchfrog 2005
- Published many papers on thyroid disruption and brain development
- Major review in 2018

Endocrine CONNECTIONS

REVIEW

Thyroid disrupting chemicals and brain development: an update

Bilal B Mughal, Jean-Baptiste Fini and Barbara Demeneix

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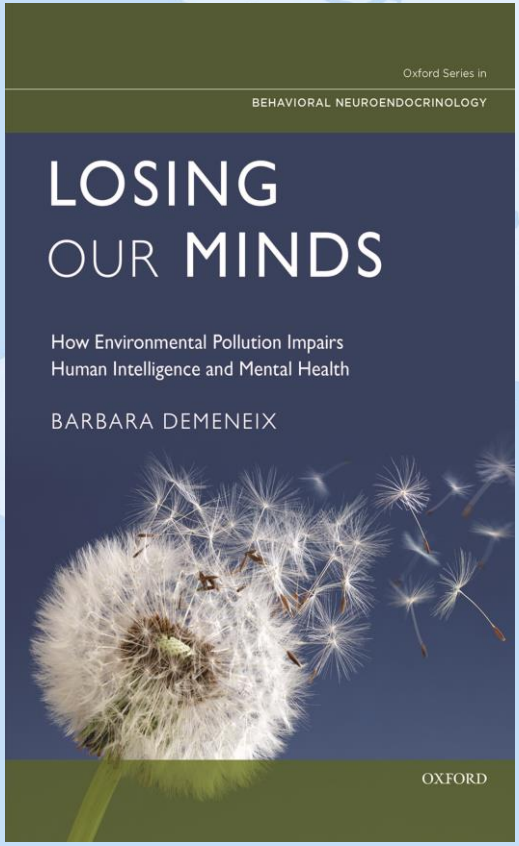
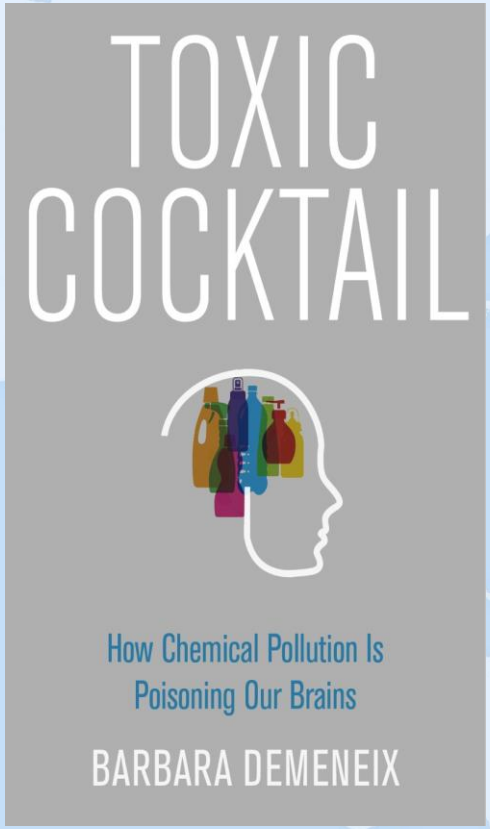
My knowledge and concern led to:

- My writing two single author books
- The CNRS medal for innovation in 2014





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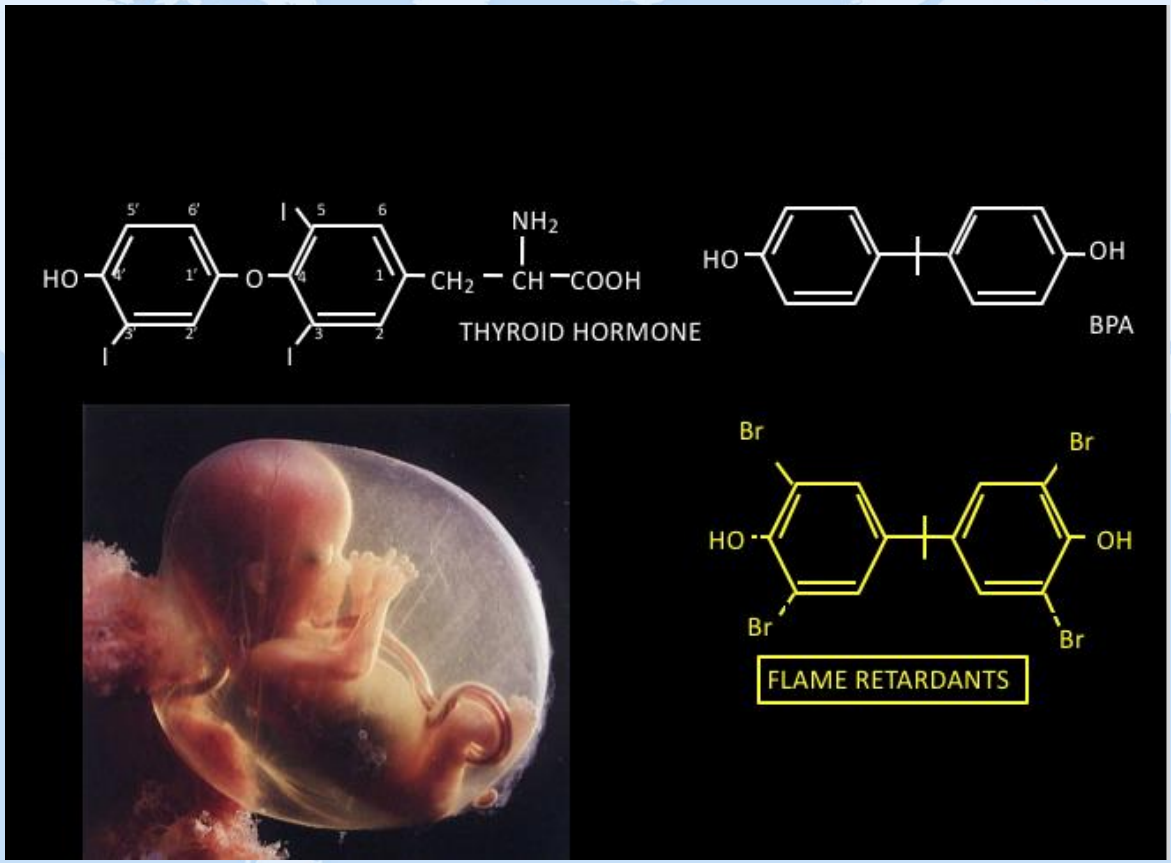
EDCs present in maternal blood are also found in amniotic fluid and affect thyroid hormone signaling



A mixture of 15 common chemicals at levels found in human amniotic fluid alter

- Thyroid hormone signaling in an animal model
- Brain gene expression
- Behaviour

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EU EDC Criteria and Guidance Document

- Gaps and uncertainties remain and need to be addressed:
  - Potential for false-negatives is high
  - Need to apply criteria to other chemicals and other endocrine systems (besides androgen, estrogen and thyroid)
  - Certain categories require **better test methods** - hence H2020 call for **screening**
  - Focus on thyroid, neurodevelopment, metabolism, female reprod, non-genomic carcinogens

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Guidance Document – Endocrine Society Statement.

- Scope of guidance is too limited
  - EDCs can act on a wide variety of receptors and pathways beyond what is covered in guidance- must eventually cover other hormone pathways involved in for example metabolism, body weight, and insulin action/secretion.
- Required level of proof too high to protect health
  - ***If an adverse effect is observed and endocrine-mediated action observed, this should be sufficient to support the definition of an EDC.***
  - In this case detailed study of ED action and mechanisms should not be required and would delay precautionary action.

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We Need Better Public Health Protection

- New scientific information has been developed since the original1999 European Strategy on EDCs
- EDCs are ubiquitous, and many potential sources of exposure are not covered in biocides and pesticides law.
- Still have gaps in cosmetics legislation and food packaging regulations

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A New Strategy is Required

- Therefore, the EU Strategy on EDCs should be rapidly updated and revised,
  - Prioritize new scientific information developed in recent years
  - Aim to minimize exposure to hazardous EDCs throughout the environment and in consumer products
- The European Commission and agencies should support further research into EDCs
  - See: Hormone disrupting chemicals: slow progress to regulation BMJ 2018; 361
    - https://doi.org/10.1136/bmj.k1876 (Published 30 April 2018)

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Additional Research is Necessary

- Example research opportunities:
  - Evaluation of EDC exposures and outcomes at different life stages
  - Research on genetic susceptibility and population-based differences in exposures and outcomes
  - Chemical mixtures, synergistic effects of chemicals, steady-state and cumulative exposures
  - Storage of EDCs in the body and effects of exercise and weight loss on EDC storage
  - Longitudinal and multigenerational studies on animals and humans
  - Epigenetics and endocrine-disruption crosstalk

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Hormone Science to Health

Regulatory implications of endocrine science

- EDC effects are complex:
  - Chemicals may have different effects on different organs, or through different mechanisms, and may have different effects (e.g., sex-specific, genetics)
  - Timing of exposure matters (e.g., fetal development, adolescence)
  - Hormones act at very low concentrations
- Regulatory agencies need to address:

  Sensitivity of single endpoints; susceptible populations and vulnerability at different developmental stages; low-dose and non-monotonic dose response

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Scientific Evidence for EDC Effects

- EDC Science has advanced rapidly in recent years.
- Increasing evidence links EDC exposure to a variety of adverse health outcomes, including obesity and diabetes, reproductive disorders, hormone-sensitive cancers, and neurodevelopmental disease

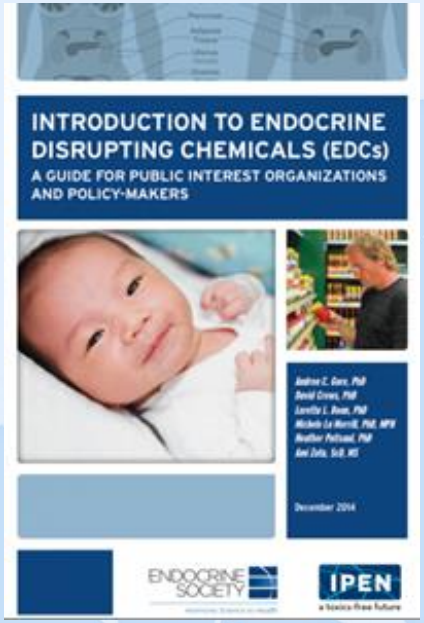
REVIEW

EDC-2: The Endocrine Society's Second Scientific Statement on Endocrine-Disrupting Chemicals

A. C. Gore, V. A. Chappell, S. E. Fenton, J. A. Flaws, A. Nadal, G. S. Prins, J. Toppari, and R. T. Zoeller

I. Introduction to EDC-2
A. Five years after the Endocrine Society's first Scientific Statement
B. Endocrine systems are a physiological interface with the environment, and gene-by-environment interactions are perturbed by EDCs
C. The developmental origins of health and disease
D. Epigenetics and transgenerational effects of EDCs
E. Dose-response characteristics of EDCs
F. Identifying effects of EDCs on human health: where to start?
G. Review criteria for EDC-2

II. Obesity, Diabetes Mellitus, and Cardiovascular Diseases
A. Introduction
B. Definition and etiology of obesity
C. Definition and etiology of type 2 diabetes mellitus
D. EDCs and type 1 diabetes mellitus
E. EDCs and cardiovascular diseases
F. Conclusions



www.endocrine.org/edc

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