

EDC Criteria and next steps: A scientific perspective

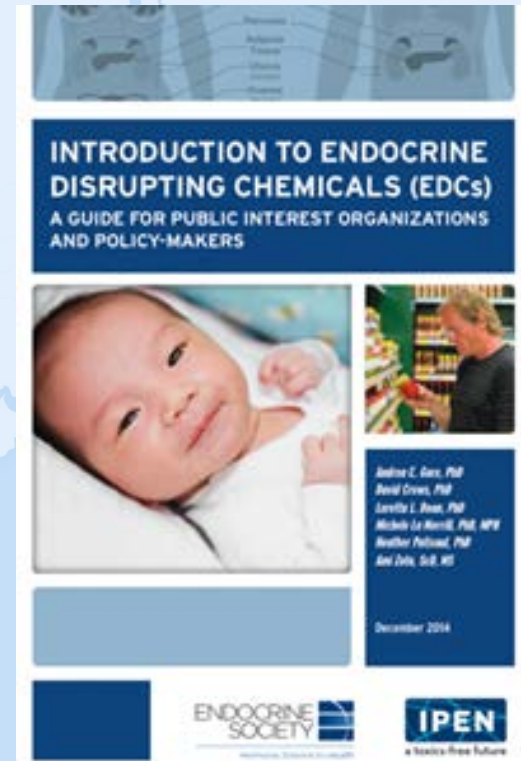
Barbara Demeneix, BSc, PhD, DSc
Chair, Endocrine Society EU Task Force

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

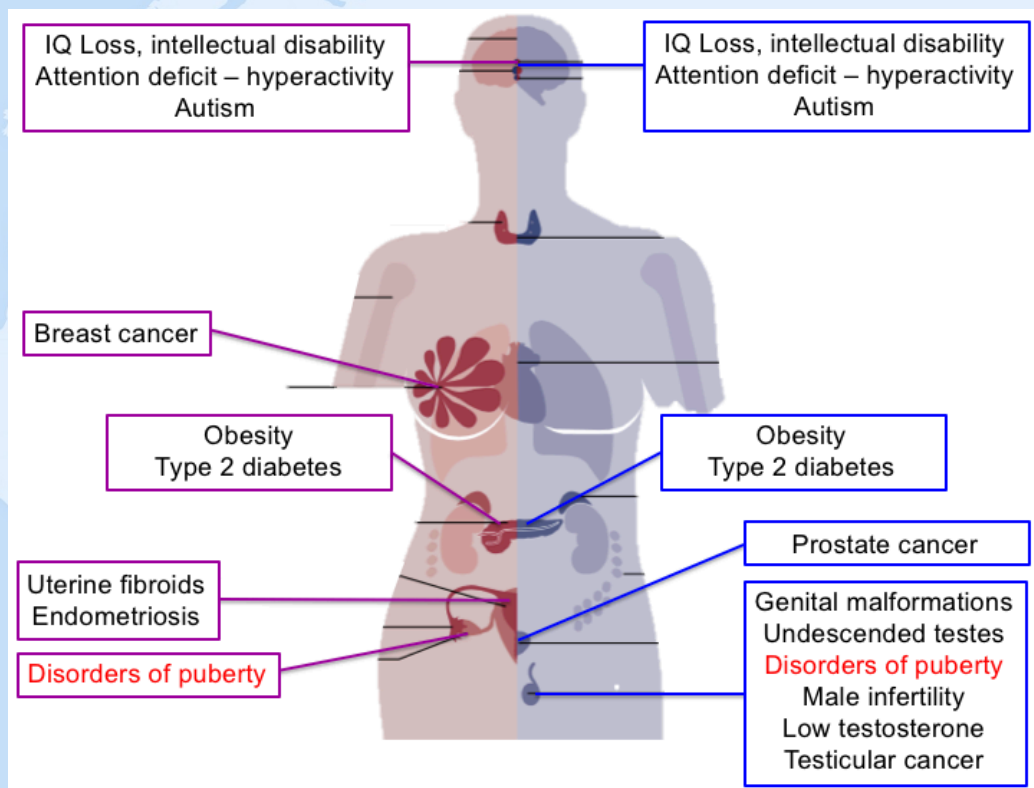
EDCs are not like other chemicals

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



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



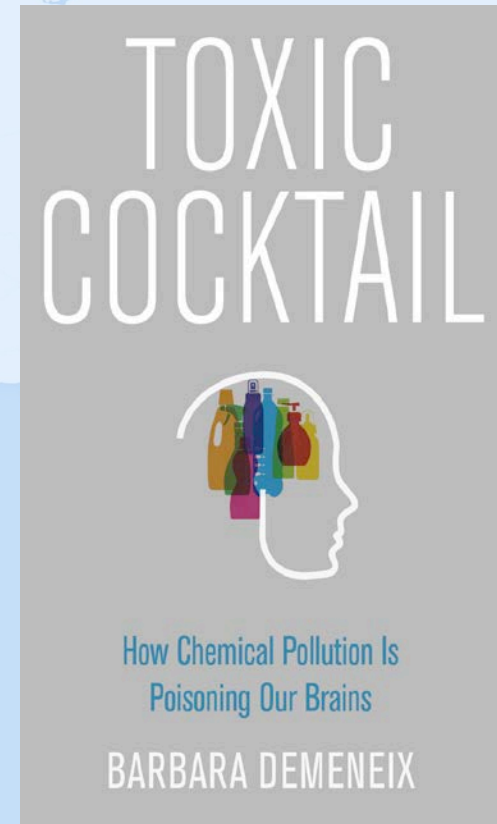
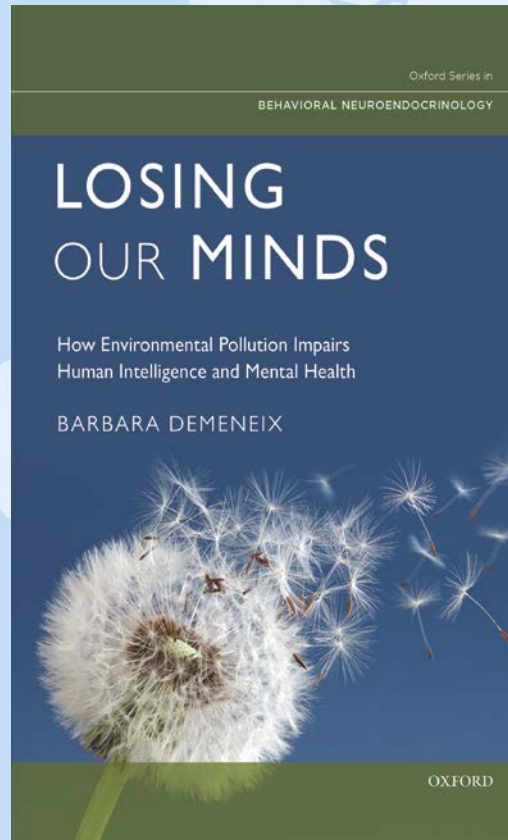
REVIEW

Thyroid disrupting chemicals and brain development: an update

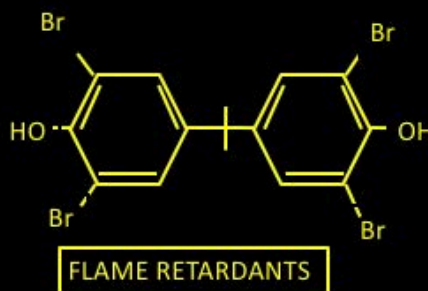
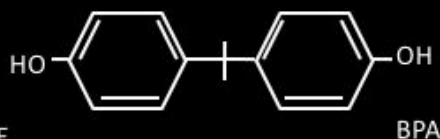
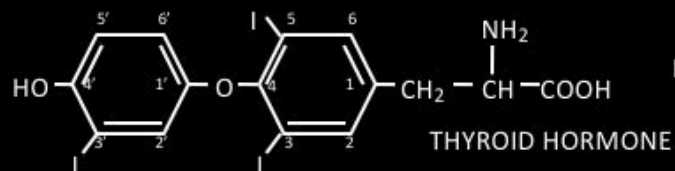
Bilal B Mughal, Jean-Baptiste Fini and Barbara Demeneix*

My knowledge and concern led to:

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



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

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

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.

We Need Better Public Health Protection

- New scientific information has been developed since the original 1999 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

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)

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

ENDOCRINE SOCIETY



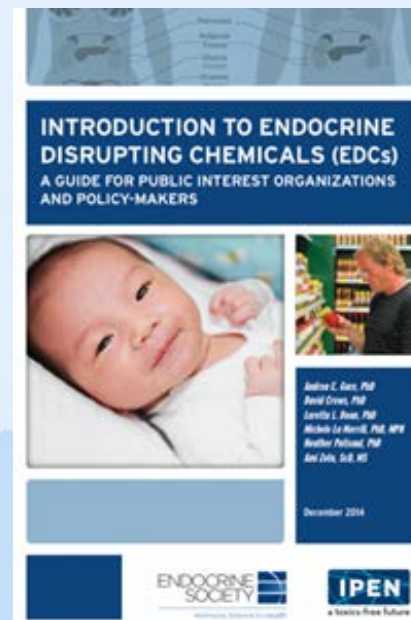
Hormone Science to Health

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

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



www.endocrine.org/edc