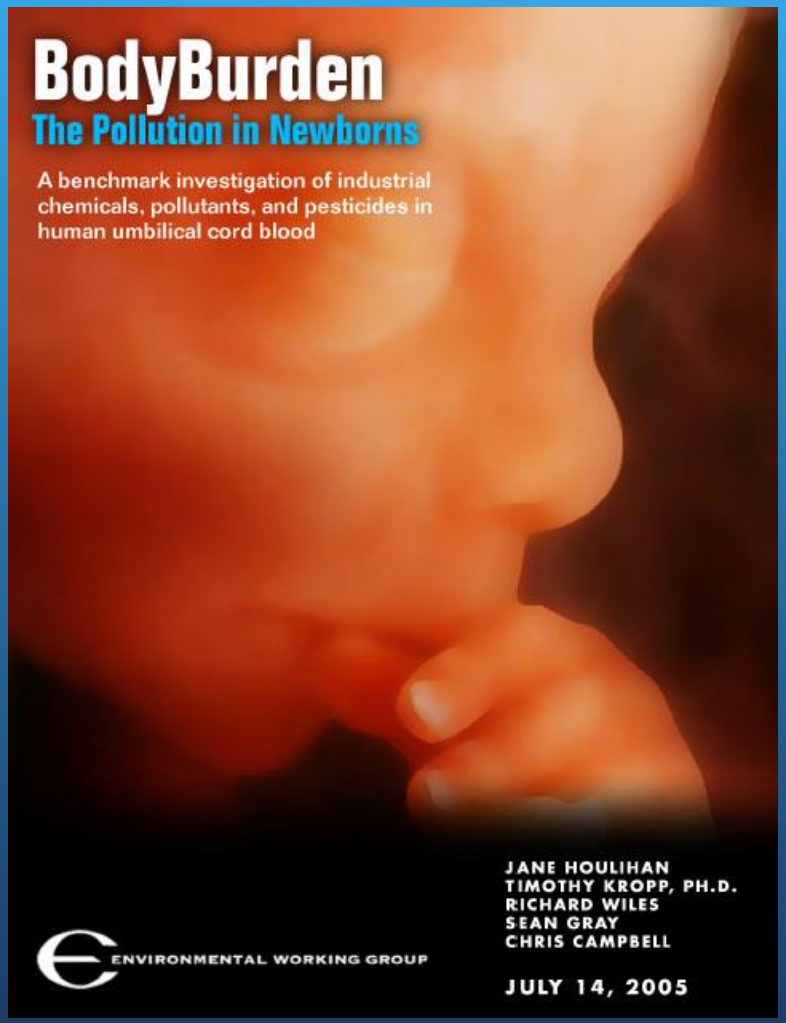
CHE Webinar

Why are we so contaminated? EDC testing, and regulations

R. Thomas Zoeller

Chemicals in the Human Population



- 287 chemicals (of 417 examined) were identified in these 10 samples, with a range of 154 – 231 for each child.
- 180 of these cause cancer in humans or animals
- 217 are neurotoxic in animals
- 208 are developmental toxins

How EDCs fall through the cracks

- EXAMPLE: POLYCHLORINATED BIPHENYLS (PCBs) AND COGNITIVE FUNCTION

- PCBs were used in many different kinds of products until they were banned by Congress in the late 1970s.

PCBs are Neurotoxicants

Table 3. Neuropsychological outcomes of human PCB studies.[a]

Test	Age	Outcome	Exposure variable	References
Congener-specific studies				
Oswego cohort				
NBAS	Birth	↓ Autonomic	7–9 chlorinated PCBs	Stewart et al. (2000)
		↓ Habituation	7–9 chlorinated PCBs	
Fagan	6 months	↓ Fixation time	Cord blood PCBs, 7–9 chlorinated PCBs	Darvill et al. (2000)
	12 months	↓ Fixation time	Cord blood PCBs	Darvill et al. (2000)
German cohort				
Fagan	7 months	No effect		Winneke et al. (1998)
Bayley scales	7 months	↓ MDI	ln ∑PCBs (138, 153, and 180) breast milk	Winneke et al. (1998)
	18 months	No effect		Walkowiak et al. (2001)
	30 months	↓ MDI	ln ∑PCBs (138, 153, and 180) breast milk	Walkowiak et al. (2001)
Kaufman ABC	42 months	↓ Mental processing composite index	ln ∑PCBs (138, 153, and 180) breast milk	Walkowiak et al. (2001)
Faroe Islands cohort				
Boston Naming Test		↓ Performance	Cord blood PCBs	Grandjean et al. (2001)
Auditory function		↑ Auditory thresholds	Cord blood PCBs	Grandjean et al. (2001)
Noncongener-specific studies				
Michigan cohort				
Birth size/growth	Birth	↓ Birth weight	Cord blood PCBs	Fein et al. (1984)
		↓ Head circumference	Cord blood PCBs	
		↓ Gestational age	Cord blood PCBs	
	5 months	↓ Body weight	Cord blood PCBs	Jacobson and Jacobson (1988)
Bayley scales	5 months	No effect		Jacobson and Jacobson (1986)
Fagan	7 months	↓ Fixation time	Cord blood PCBs	Jacobson et al. (1985)
McCarthy scales	4 years	↓ Verbal memory	Cord blood PCBs, breast milk PCBs	Jacobson et al. (1990a)
		↓ Numerical memory	Cord blood PCBs, breast milk PCBs	
		↓ Visual discrimination	Breast milk PCBs	Jacobson et al. (1992)
		↓ Short term memory	Cord blood PCBs	
Birth size/growth	4 years	↓ Body weight	Total cord PCBs	Jacobson et al. (1990b)
		↓ Activity	Child's total PCBs	
WISC-R	11 years	↓ Full-scale IQ	Prenatal PCBs	Jacobson and Jacobson (1996)
		↓ Verbal IQ	Prenatal PCBs	
North Carolina cohort				
NBAS	Birth	↓ Muscle tone	Breast milk PCBs	Rogan et al. (1986b)
		↓ Activity	Breast milk PCBs	
		↓ Reflexes	Breast milk PCBs	
Bayley scales	6 months	↓ PDI	Breast milk PCBs	Gladen et al. (1988)
	12 months	↓ PDI	Breast milk PCBs	Gladen et al. (1988)
	18 months	No effect		Rogan and Gladen (1991)
	24 months	↓ PDI	Breast milk PCBs	Rogan and Gladen (1991)
McCarthy scales	3–5 years	No effect		Gladen and Rogan (1991)

Abbreviations: ↓, decrease; ↑, increase; Bayley scales, Bayley Scales of Infant Development; Fagan, Fagan Test of Infant Intelligence; Kaufman ABC, Kaufman Assessment Battery for Children; McCarthy scales, McCarthy Scales of Children's Abilities; NBAS, Brazelton Neonatal Behavioral Assessment Scale; Wisc-R, Wechsler Intelligence Scales for Children-Revised. [a]Dutch cohort is summarized in Table 2.

Is the Cognitive Effect of PCBs Mediated by an Endocrine Mechanism?

- Proposal: PCBs cause a reduction in serum thyroid hormone, leading to cognitive deficits when present during specific periods of development.
- PCB exposure in animals uniformly causes a reduction in serum thyroid hormone
- Some PCB congeners can bind to the thyroid hormone receptor in vitro and this could explain some effects of PCBs in humans

Is the Cognitive Effect of PCBs Mediated by an Endocrine Mechanism?

- Proposal: PCBs cause a reduction in serum thyroid hormone, leading to cognitive deficits when present during specific periods of development.
- BUT: Epidemiological studies do not uniformly find that environmental levels of PCBs are linked to lower levels of PCBs.
- So, while it is widely accepted that PCBs produce cognitive deficits in humans, their “status” as human EDCs could be argued.

Tier 1 Assays have been around for 50+ years. These assays did not identify PCBs adverse effects in the '60's and 70's. Why would they now?

Table 1 Assays included in the U.S. EPA's Tier 1 Screening Battery

In Vitro

- *Estrogen receptor binding*
- *Estrogen receptor transcriptional activation*
- *Androgen receptor binding*
- *Steroidogenesis (H295R)*
- *Aromatase (human recombinant)*

In vivo

- *Utererotropic*
- *Hershberger*
- *Pubertal rat male*
- *Pubertal rat female*
- *Fish short-term reproduction*
- *Amphibian metamorphogenesis*

Why are we so contaminated?

- 1. Weak Laws (for both EPA and for FDA food safety)
- 2. Weak strategy for assessing EDC risk.

Guideline Endpoints

- Government approved toxicity tests ("Guideline Studies") capture body and organ weight and histopathology when weight is reduced.
- Measurements do not "map" to effects observed in the human population

Several Major Publications all conclude that testing for EDCs is not adequate!

POSITION STATEMENT

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

Biology Department and Molecular and Cellular Biology Program (R.T.Z.), University of Massachu
Amherst, Massachusetts 01003; Johns Hop
Maryland 21205; The Endocrine Society (L

REVIEW

Hormones and Endocrine-Disrupting Chemicals: Low-Dose Effects and Nonmonotonic Dose Responses

Laura N. Vandenberg, Theo Colborn, Tyrone B. Hayes, Jerrold J. Heindel, David R. Jacobs, Jr., Duk-Hee Lee, Toshi Shioda, Ana M. Soto, Frederick S. vom Saal, Wade V. Welshons, R. Thomas Zoeller, and John Peterson Myers

Center for Regenerative and Developmental Biology and Department of Biology (L.N.V.), Tufts University, Medford, Massachusetts 02155; The Endocrine Disruption Exchange (T.C.), Paonia, Colorado 81428; Laboratory for Integrative Studies in Amphibian Biology (T.B.H.), Molecular Toxicology, Group in Endocrinology, Energy and Resources Group,

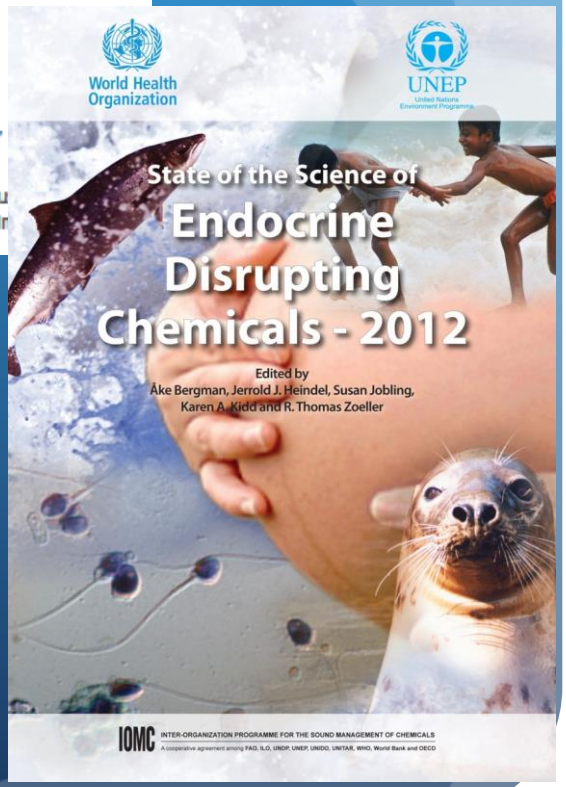
STATE OF THE ART ASSESSMENT OF ENDOCRINE DISRUPTERS

Final Report

Project Contract Number
070307/2009/550687/SER/D3

Authors: Andreas Kortenkamp, Olwenn Martin, Michael Faust, Richard Evans, Rebecca McKinlay, Frances Orton and Erika Rosivatz

23.12.2011



Conclusions

- Modern science is largely ignored in risk assessments.
  - In part, this is because the quality of primary papers is assessed by experts in fields other than the field that is the focus of the contribution.
  - In part, this is because basic science authors do not have the kind of reporting requirements that regulators appear to need.
  - This leads to a situation where the evidence of “adverse effect” is primarily the guideline studies using organ weight as a metric.
  - Public health is not protected.