ENDOCRINE DISRUPTING CHEMICALS IN INDOOR ENVIRONMENTS AND HUMAN HEALTH RISKS

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State of the Science of

Endocrine Disrupting Chemicals 2012

Summary for Decision-Makers

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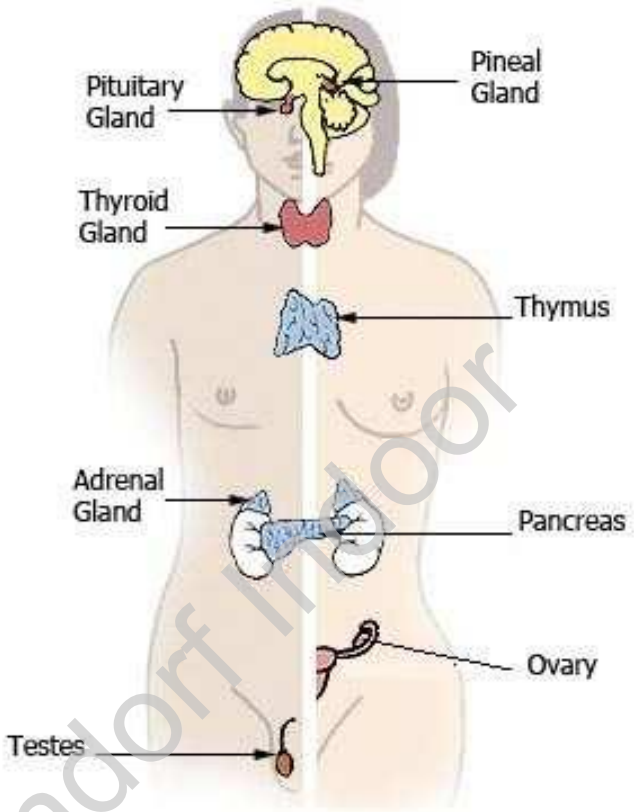
Global concern!

IOMC INTER-ORGANIZATION PROGRAMME FOR THE SOUND MANAGEMENT OF CHEMICALS
A cooperative agreement among FAO, ILO, UNDP, UNEP, UNIDO, UNITAR, WHO, World Bank and OECD

Content

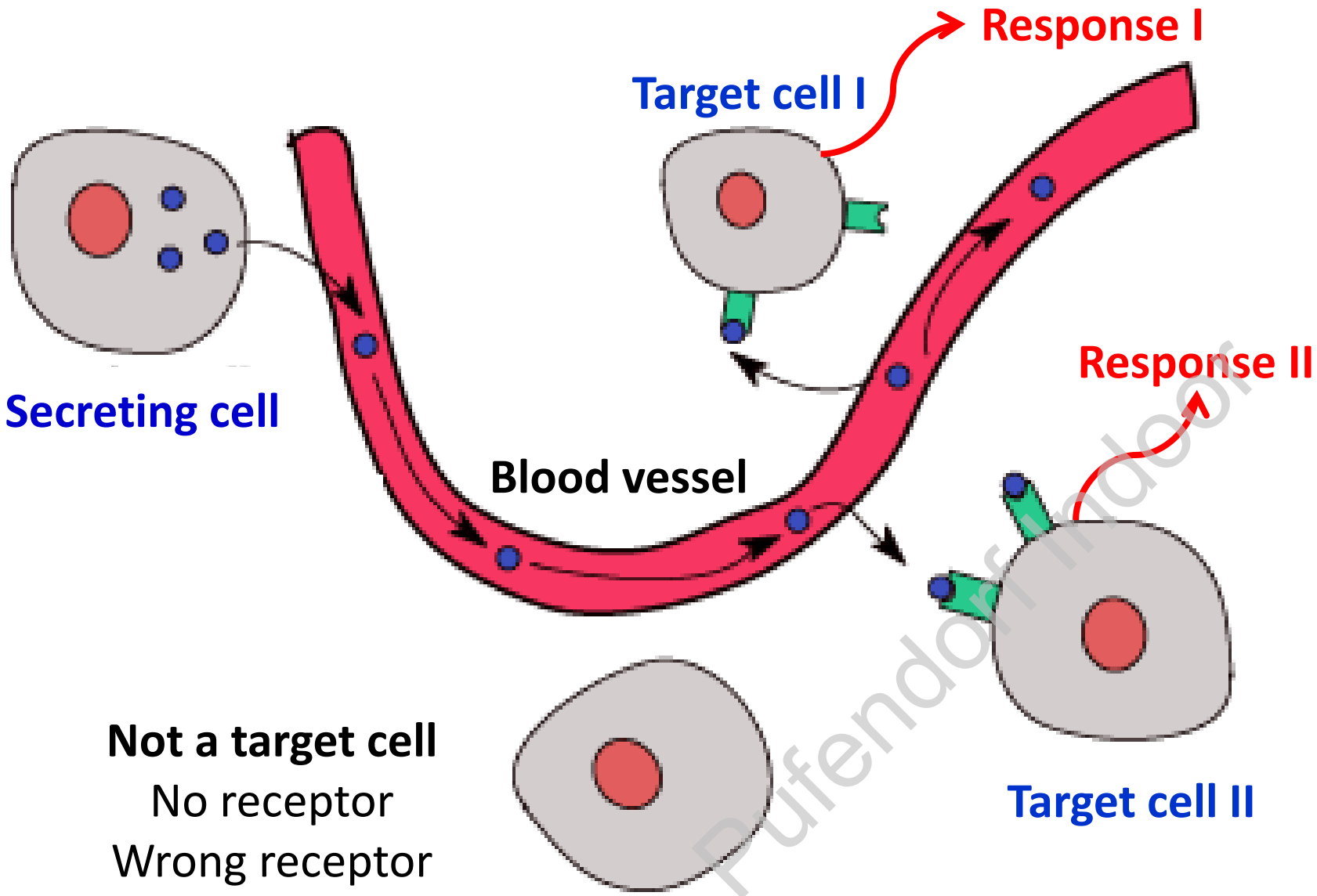
- What is an endocrine disruptor?
- Why do we concern about such exposure?
- What are we doing in the Swedish SELMA study?
  - Reproduction and sexual development

In order to understand endocrine disrupting chemicals it might be good to learn what we know about our natural endocrine system

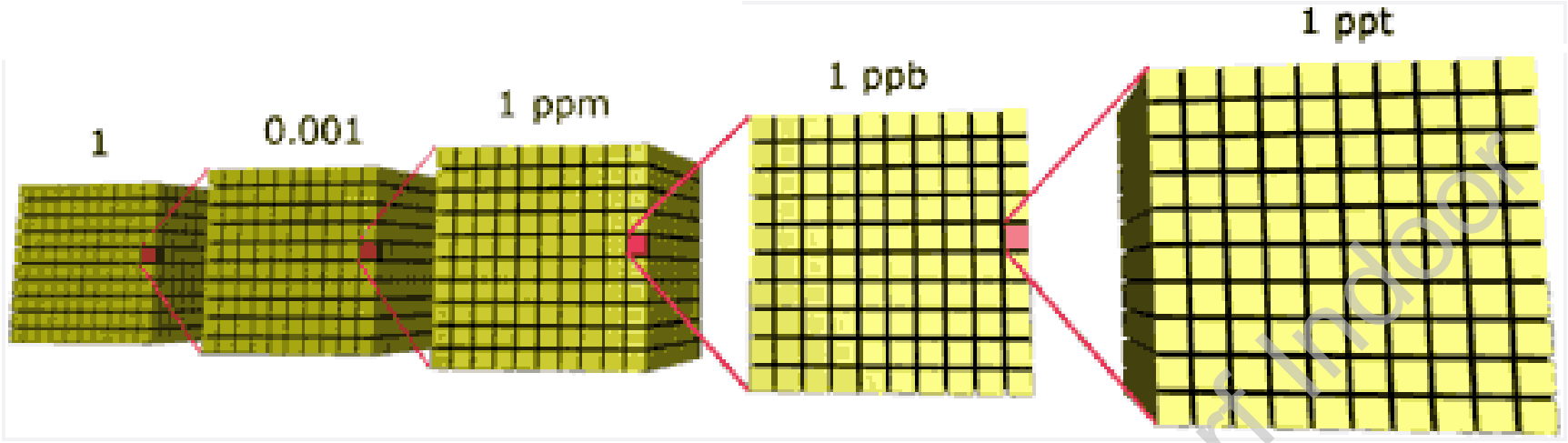


Our natural hormones are of the greatest importance for a healthy development during the entire life span from the moment of conception until death

Hormones are receptor specific



Hormones acts at very low concentrations

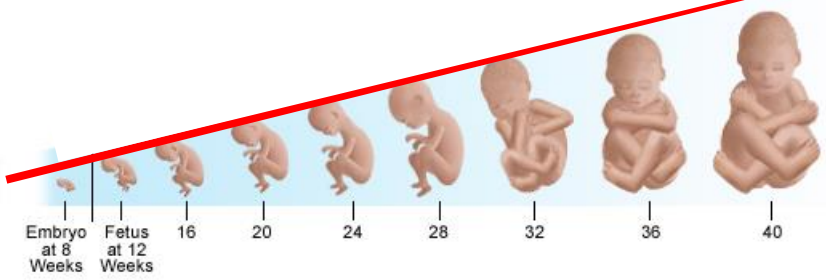


Hormones are life stage dependent

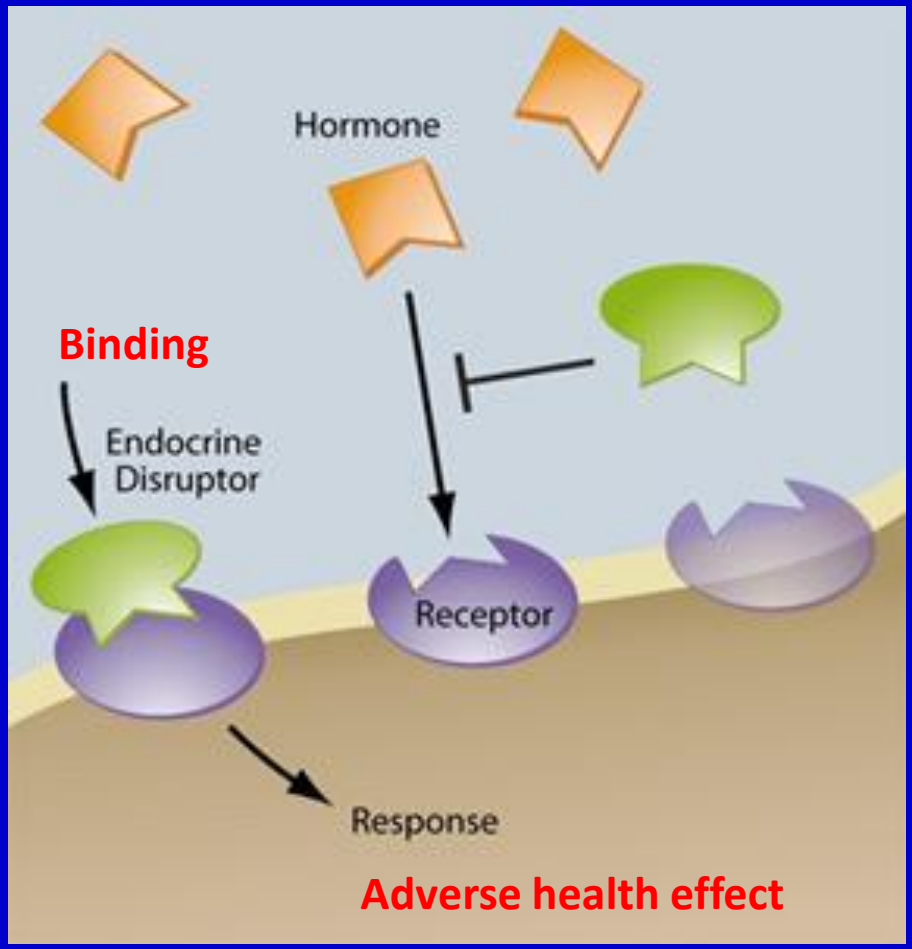
Example of <u>estrogen</u> exposure

Developmental programming (irreversible)

Reversible effects



Endocrine Disrupting Chemicals (EDCs)



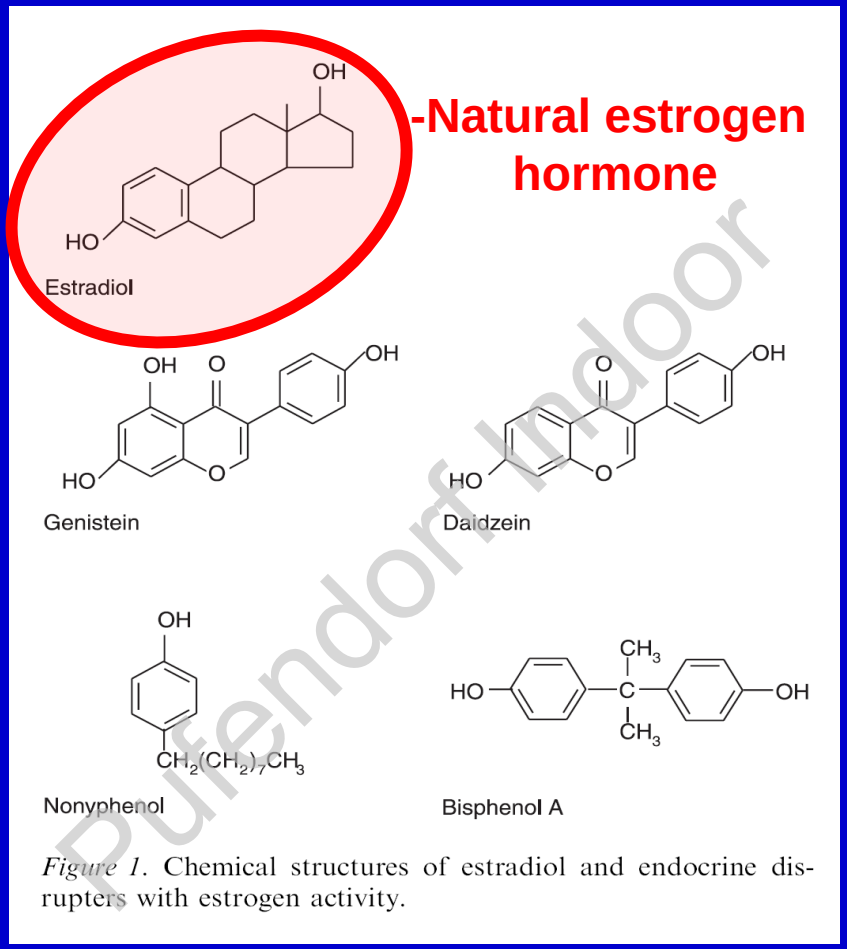


Figure 1. Chemical structures of estradiol and endocrine disrupters with estrogen activity.

Four reasons for emerging public health concern for EDC-exposure

Low doses/non-monotonic

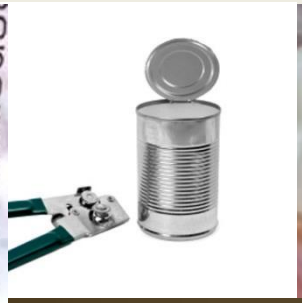
Early life is important

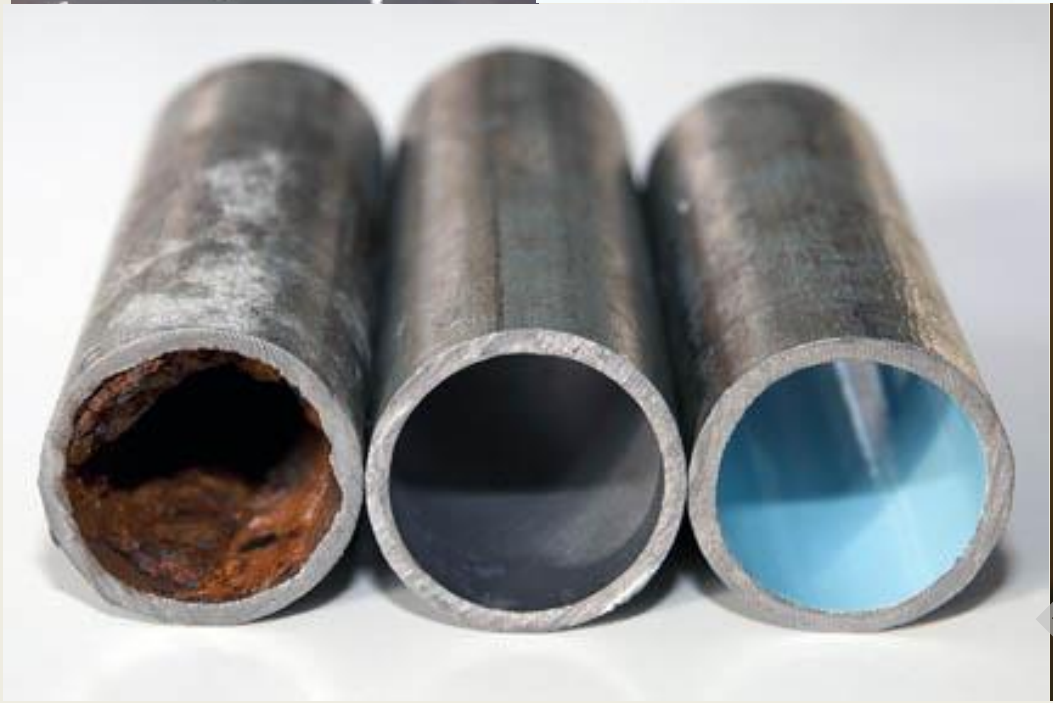
The ubiquity of exposure

The wide range of health effects

The low dose controversy

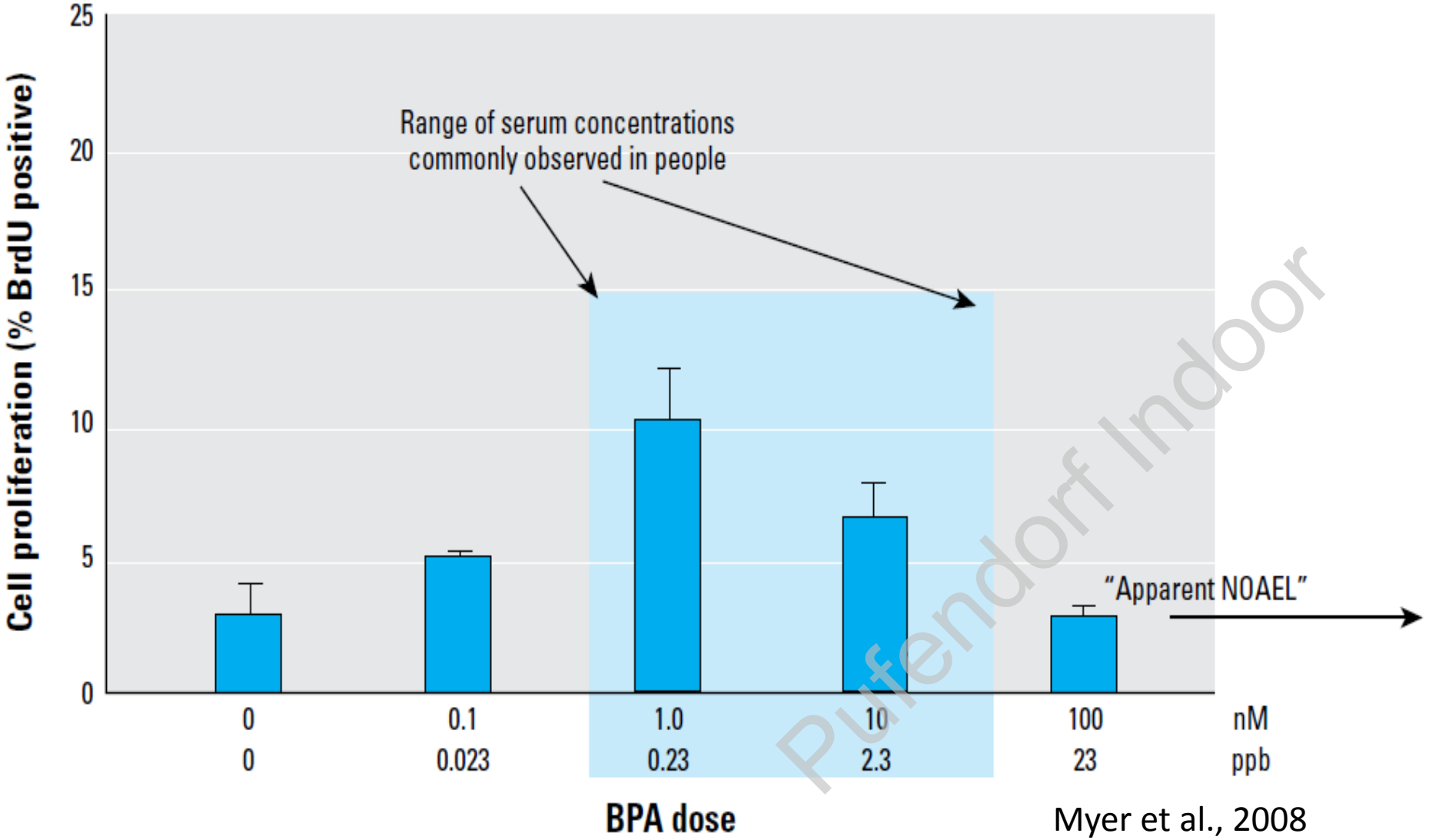
exemplified by bisphenol A





The low dose controversy

exemplified by bisphenol A



Myer et al., 2008

The dose-response paradigm

1493-1541

Phillippus
Aureolus
Theophrastus
Bombastus
von Hohenheim
Paracelsus

Response

Dose

Regulatory science

1493-1541

Response

MTD

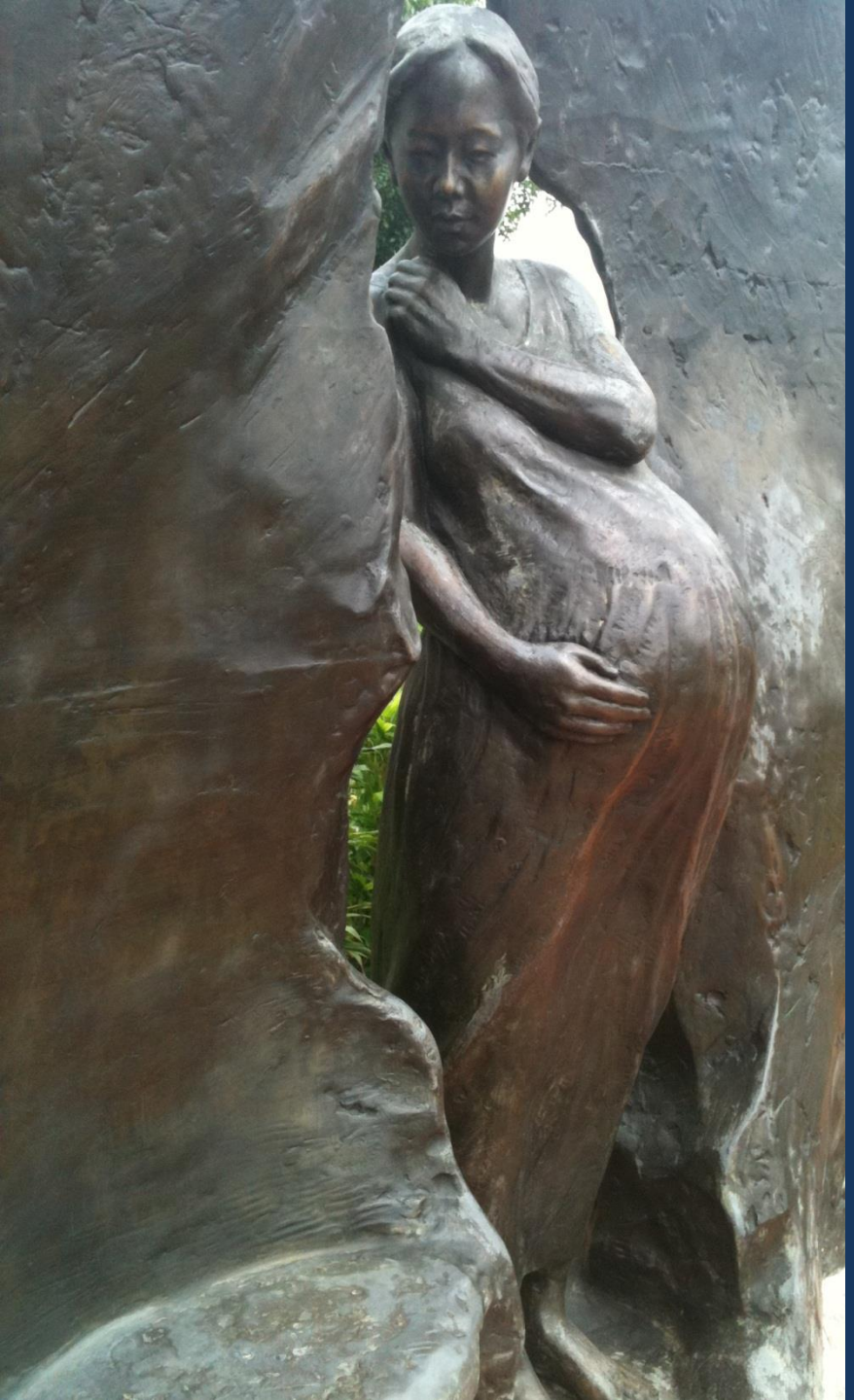
LOAEL

NOAEL

Safe dose

Safety factors

Dose

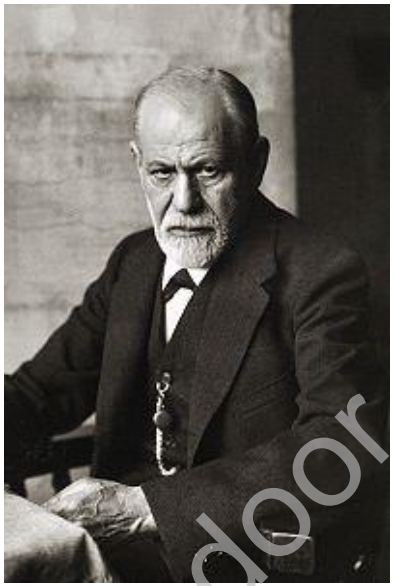


Fetal life is important due to development and programming effects

Early life is important

Sigmund Freud (1856-1939)

Early childhood experiences impacts behavior later on in life



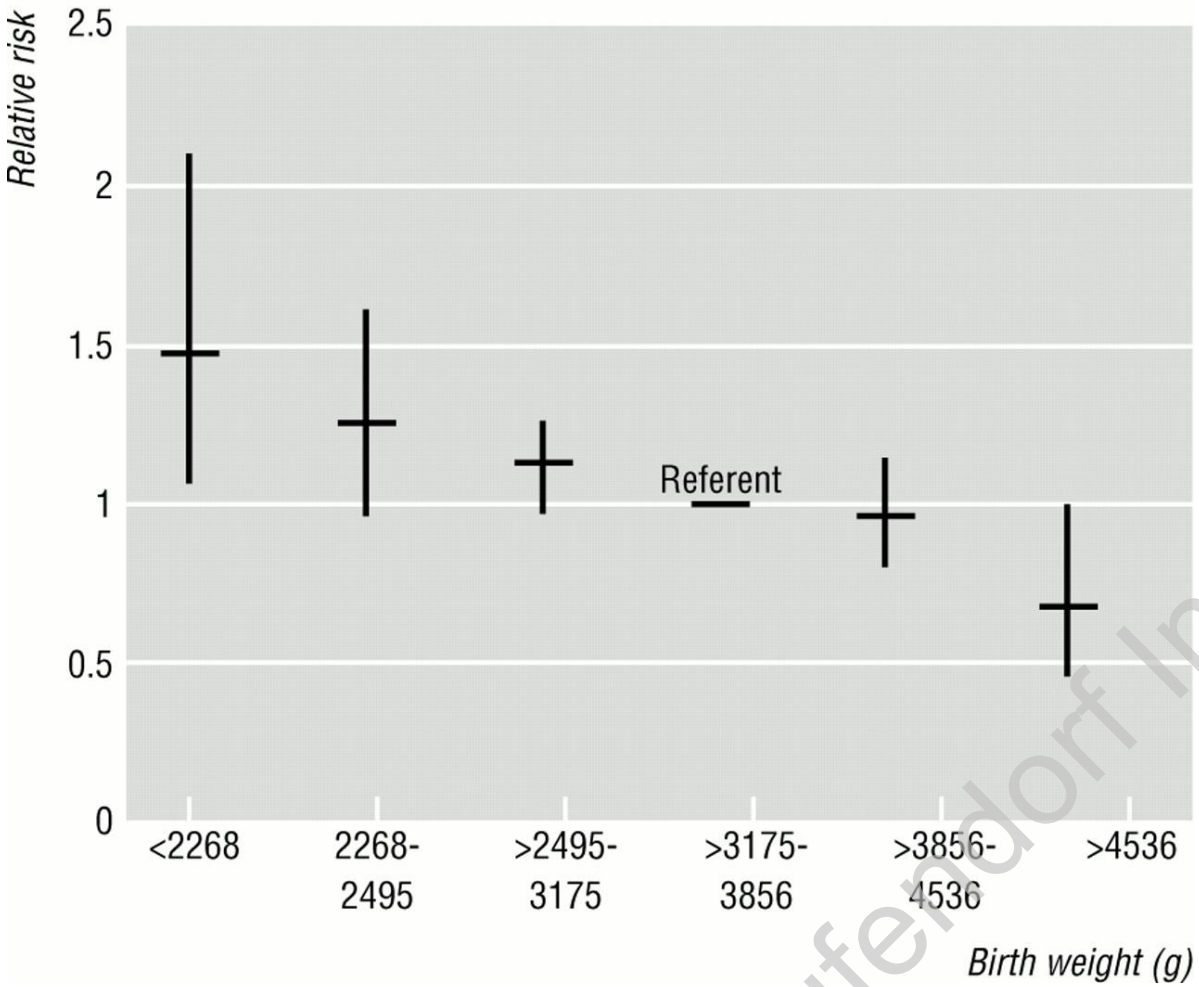
David Barker (1938-2013)

The fetal period is important for chronic diseases later on in life,

e.g., hypertonia, diabetes, cardiovascular diseases...

Birth weight

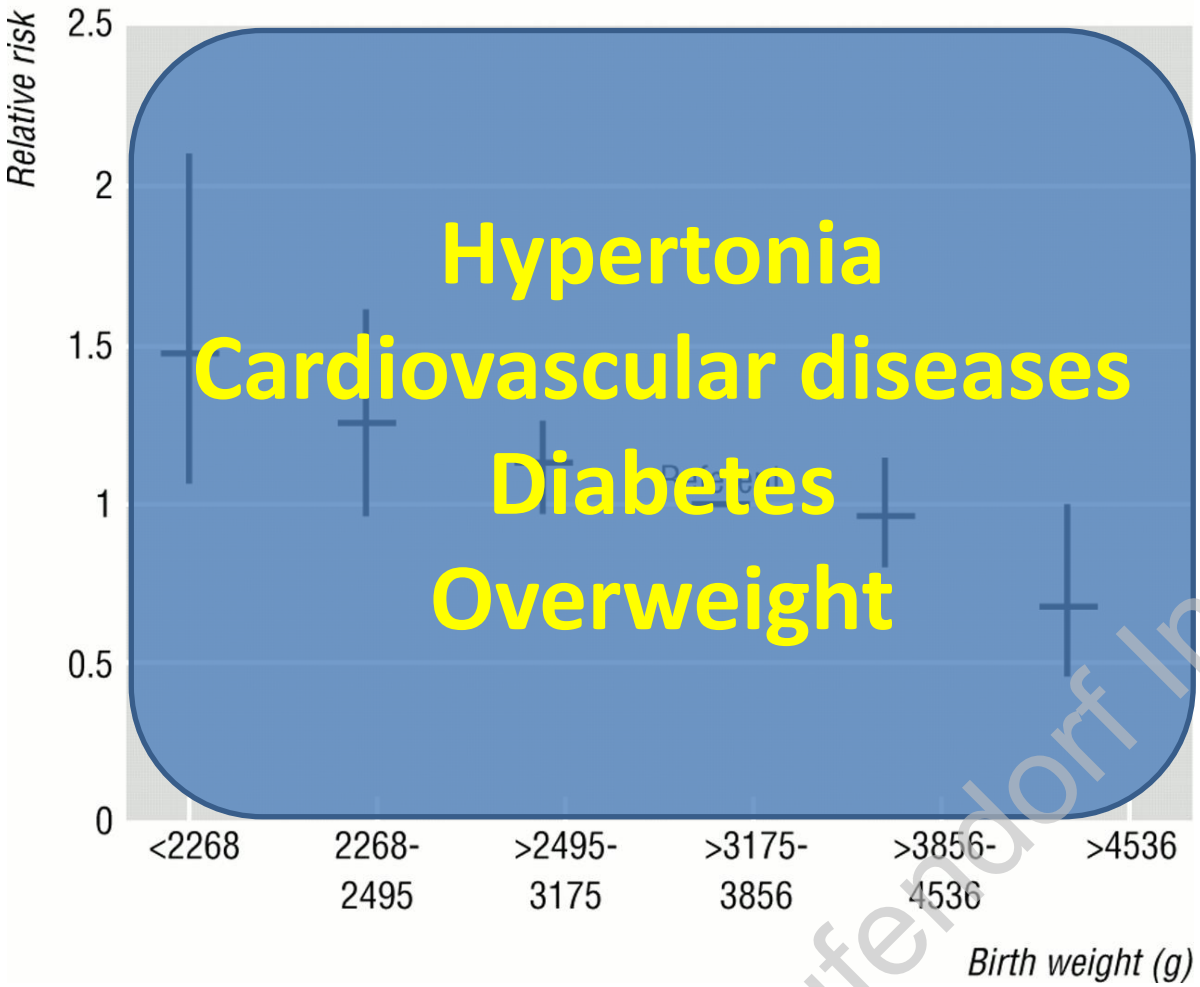
Birth weight and the risks for non-fatal cardiovascular disease



Rich-Edwards J W et al. BMJ 1997;315:396-400

BMJ

Birth weight and the risks for non-fatal cardiovascular disease



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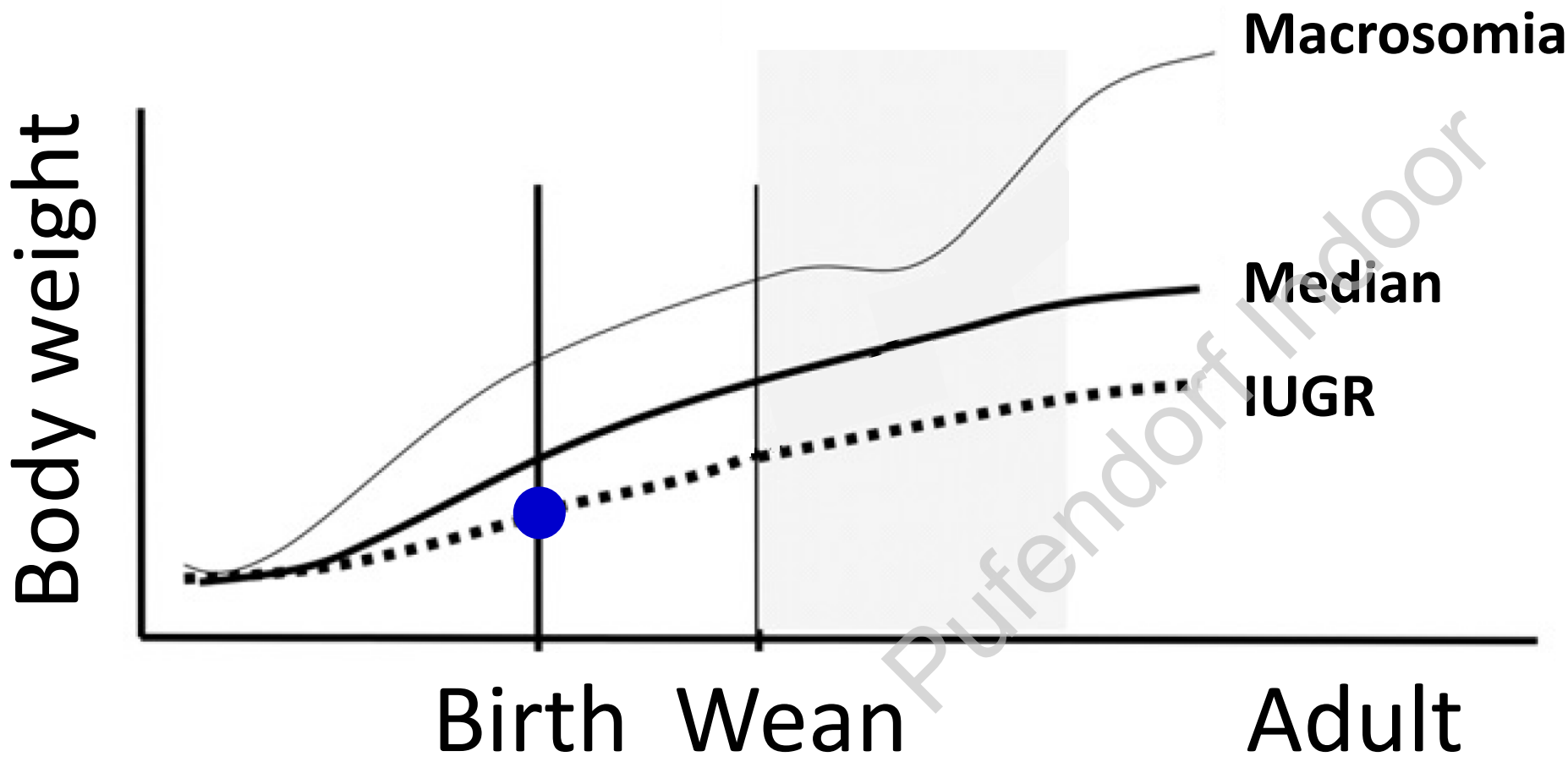
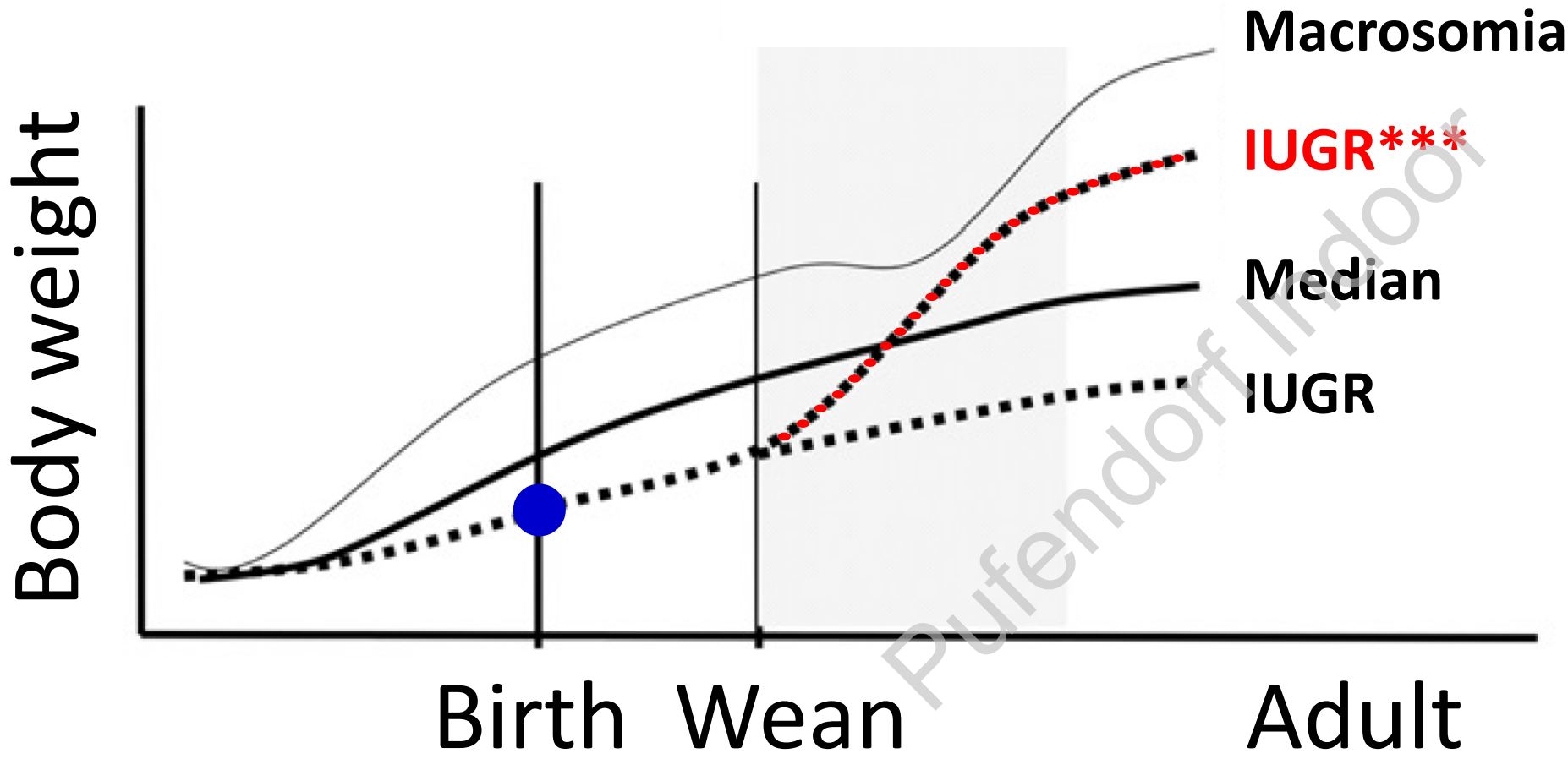
BMJ

Low birth weight



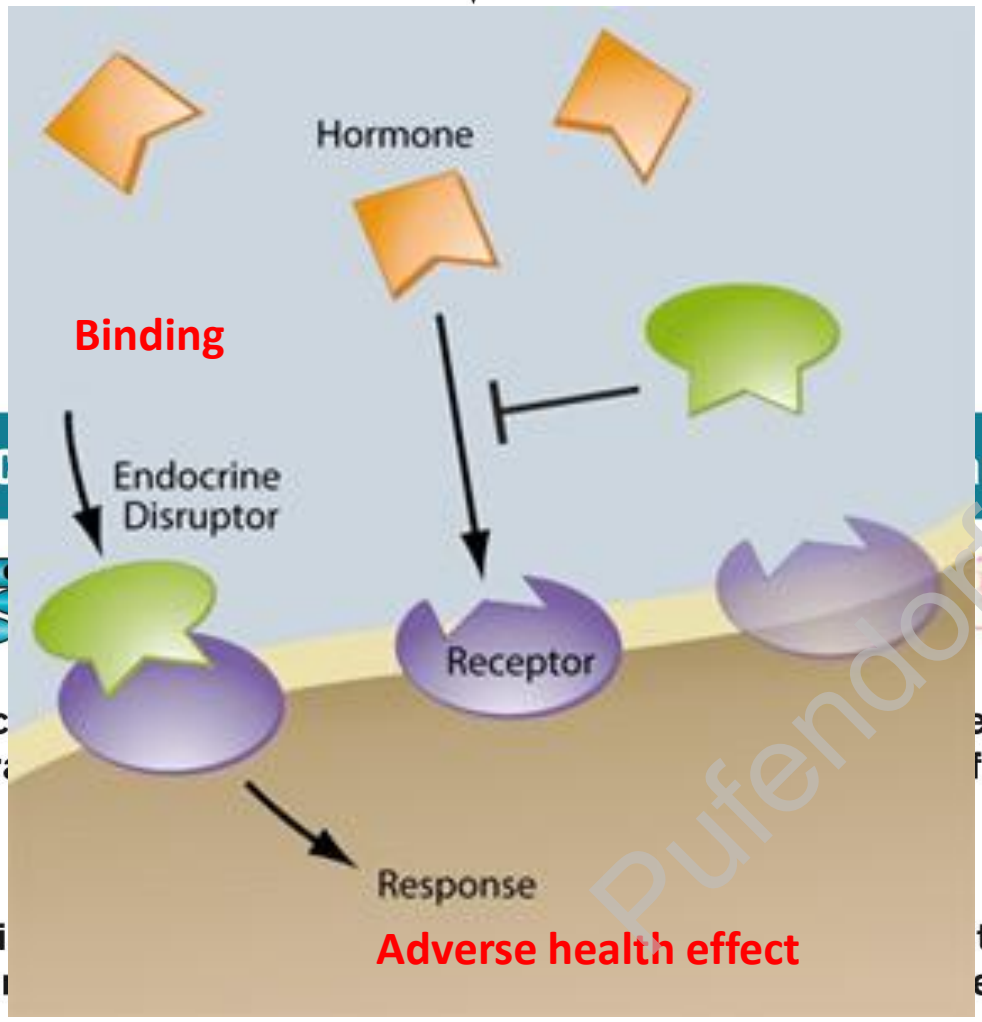
Low birth weight & Centile crossing



Mechanisms of developmental programming

(Ross & Desai 2013)

Fetal nutrition, stress, environmental toxins



Altered c
prolifer
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function
Altered i
orga
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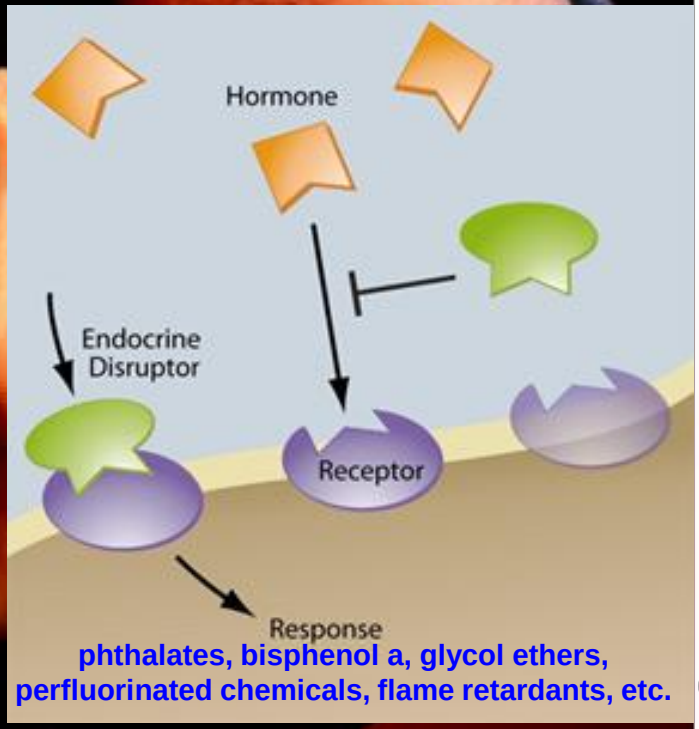
Sources for EDCs are everywhere…

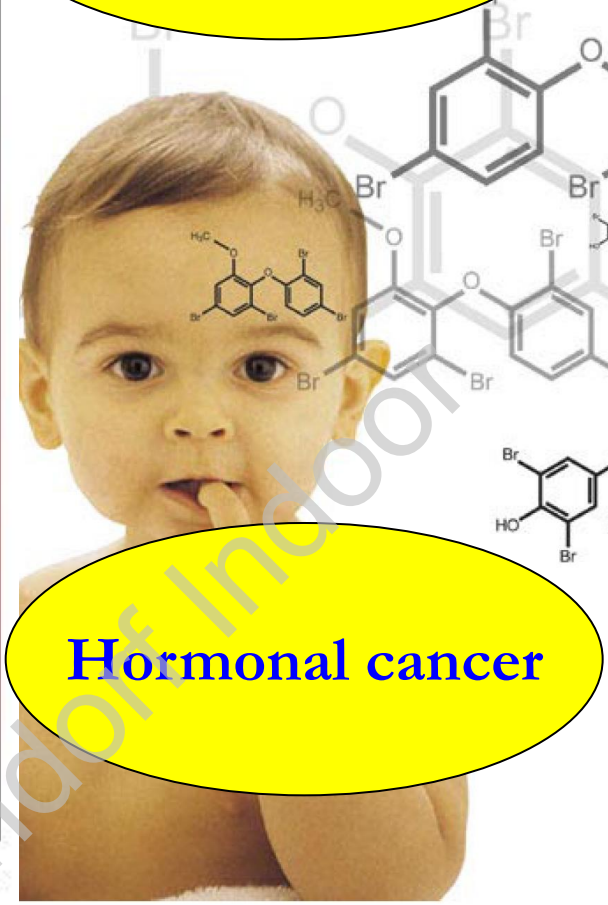
Immunological effects

Reproductive health



phthalates, bisphenol a, glycol ethers, perfluorinated chemicals, flame retardants, etc.

Metabolic syndrom incl. diabetes



Hormonal cancer

Developmental neurotoxicology

ginning a lifetime of vulnerability. A recen … that *in* …ro exposures to endocrine-disrupting chemicals … life.

Time for a Paradigm Shift?

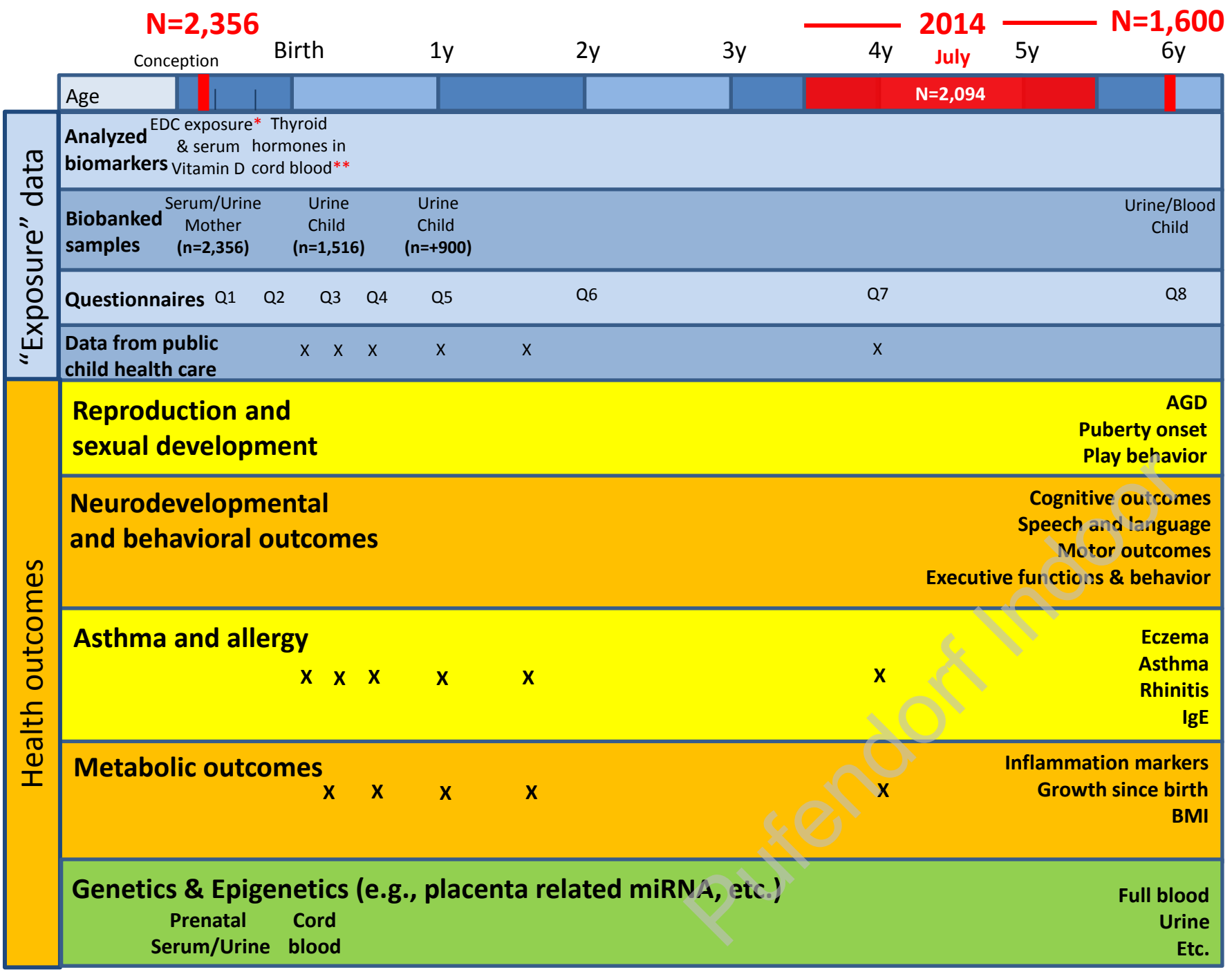
Vandenberg et al., 2013, Reproductive Toxicology

Regulatory decision and research on EDCs have to be based on principles of endocrinology!

SELMA

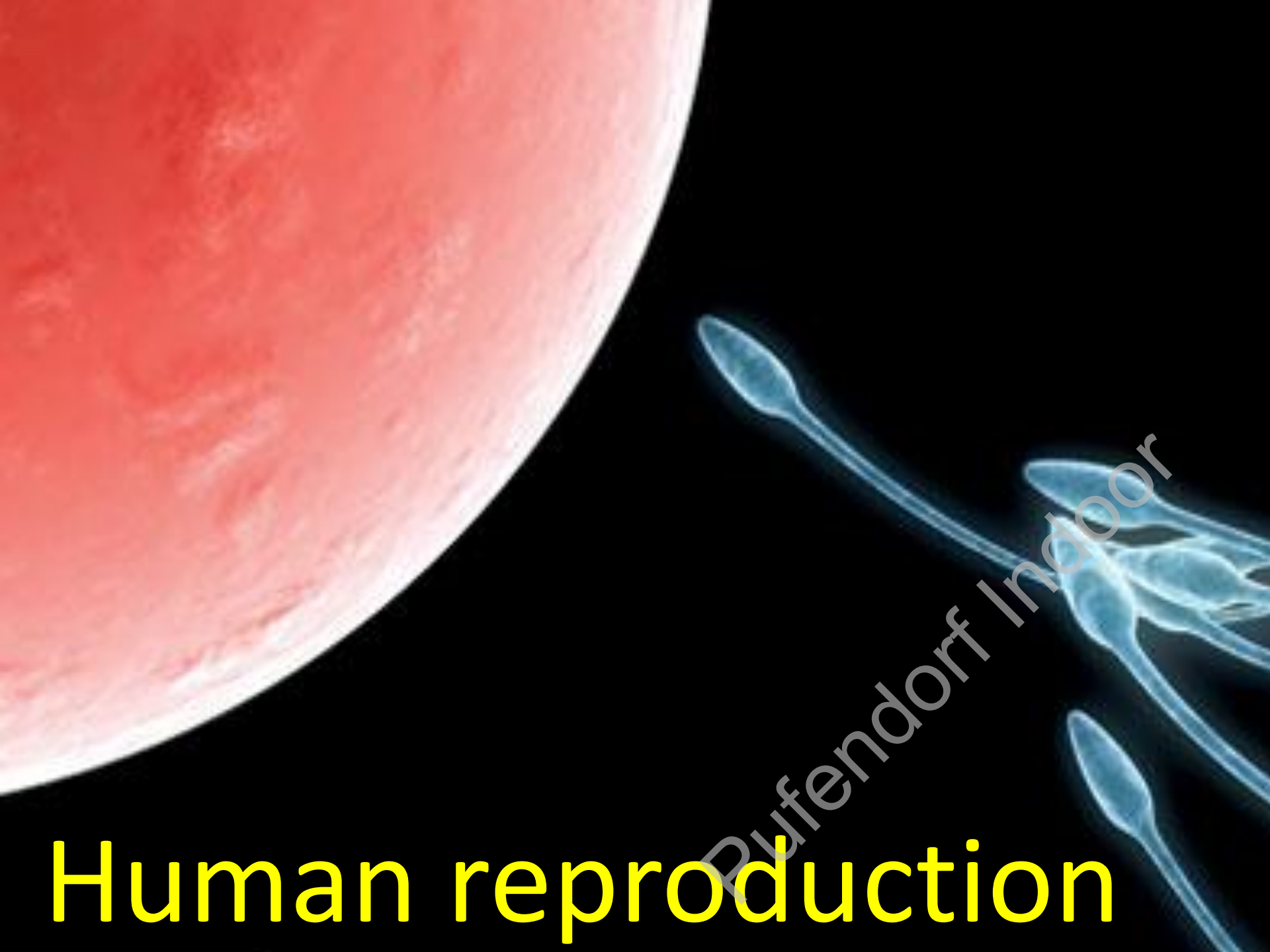
Research for a healthier future

Swedish Environmental Longitudinal, Mother and child, Asthma and allergy study


N=2,356
2014
July
N=1,600
Conception
Birth
1y
2y
3y
4y
5y
6y
Age
N=2,094
"Exposure" data
Analyzed biomarkers
EDC exposure* & serum Vitamin D
Thyroid hormones in cord blood**
Biobanked samples
Serum/Urine Mother (n=2,356)
Urine Child (n=1,516)
Urine Child (n=+900)
Urine/Blood Child
Questionnaires
Q1
Q2
Q3
Q4
Q5
Q6
Q7
Q8
Data from public child health care
X X X X X X
Health outcomes
Reproduction and sexual development
AGD
Puberty onset
Play behavior
Neurodevelopmental and behavioral outcomes
Cognitive outcomes
Speech and language
Motor outcomes
Executive functions & behavior
Asthma and allergy
X X X X X X
Eczema
Asthma
Rhinitis
IgE
Metabolic outcomes
X X X X X
Inflammation markers
Growth since birth
BMI
Genetics & Epigenetics (e.g., placenta related miRNA, etc.)
Prenatal Serum/Urine
Cord blood
Full blood
Urine
Etc.
Pufendorf Indoor

Group	Parent compound	Metabolite	n>LOD	GM (95% CI) (ng/mL)	95% (ng/mL)
Phthalates (urine)	DEP	MEP	2,356	67.97 (60.30 - 76.60)	511.49
	DBP	MBP	2,356	63.99 (57.32 - 70.94)	236.03
	BBzP	MBzP	2,356	16.11 (14.17 - 18.32)	101.59
	DEHP	MEHP	2,356	3.28 (2.98 - 3.61)	17.30
		MEHHP	2,356	14.49 (13.2 - 15.8)	67.57
		MEOHP	2,356	9.75 (8.86 - 10.68)	46.33
		MECCP	2,356	14.28 (13.03 - 15.58)	65.30
	DiNP	OH-MMeOP	2,356	6.82 (6.14 - 7.58)	60.18
		7OXO-MMeOP	2,356	3.06 (2.81 - 3.34)	20.92
		7CX-MMeOP	2,356	10.84 (10.00 - 11.75)	78.31
Phenols (urine)	Phenols	BPA	2,356	1.54 (1.48 - 1.61)	6.37
		Triclosan	2,356	0.75 (0.61 - 1.18)	315.41
Perfluorinated compounds (serum)	PFCs	PFNA	2,372	0.54 (0.53 - 0.54)	
		PFDA	2,373	0.26 (0.25 - 0.26)	
		PFUnDA	2,373	0.21 (0.20 - 0.21)	
		PFDoDA	2,344	0.03 (0.02 - 0.03)	
		PFHxS	2,373	1.31 (1.29 - 1.33)	
		PFHpA	2,297	0.02 (0.02 - 0.02)	
		PFOA	2,373	1.61 (1.58 - 1.63)	
		PFOS	2,373	5.24 (5.17 - 5.32)	

100%!!!! of 2,356 pregnant women are exposed, data from the SELMA study

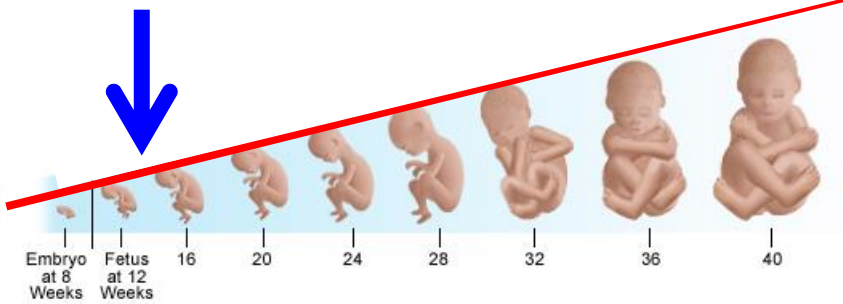


Human reproduction

Natural sexual hormones

Estrogen

Testosterone



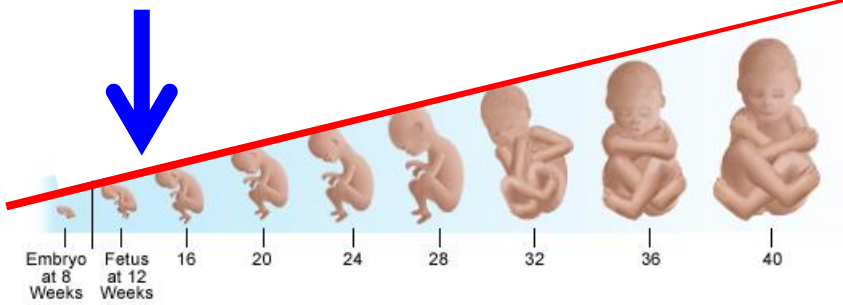
Sexual development & fertility

Chemicals with endocrine disrupting properties “Xenoestrogens”

?

Natural sexual hormones

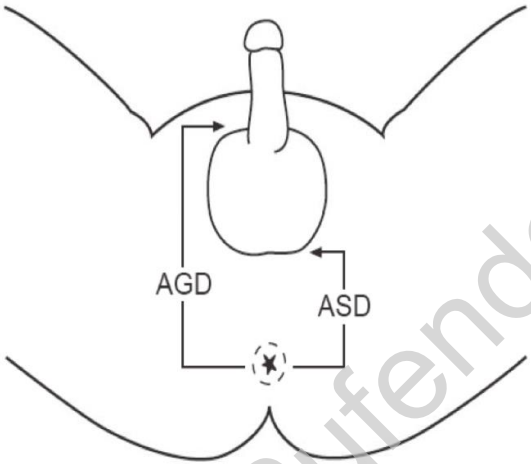
Estrogen
Testosterone



Sexual development & fertility

Chemicals with endocrine disrupting properties "Xenoestrogens"

AGD measures in male infants



196 boys in SELMA at 21 months of age

ehp ENVIRONMENTAL HEALTH PERSPECTIVES
http://www.ehponline.org

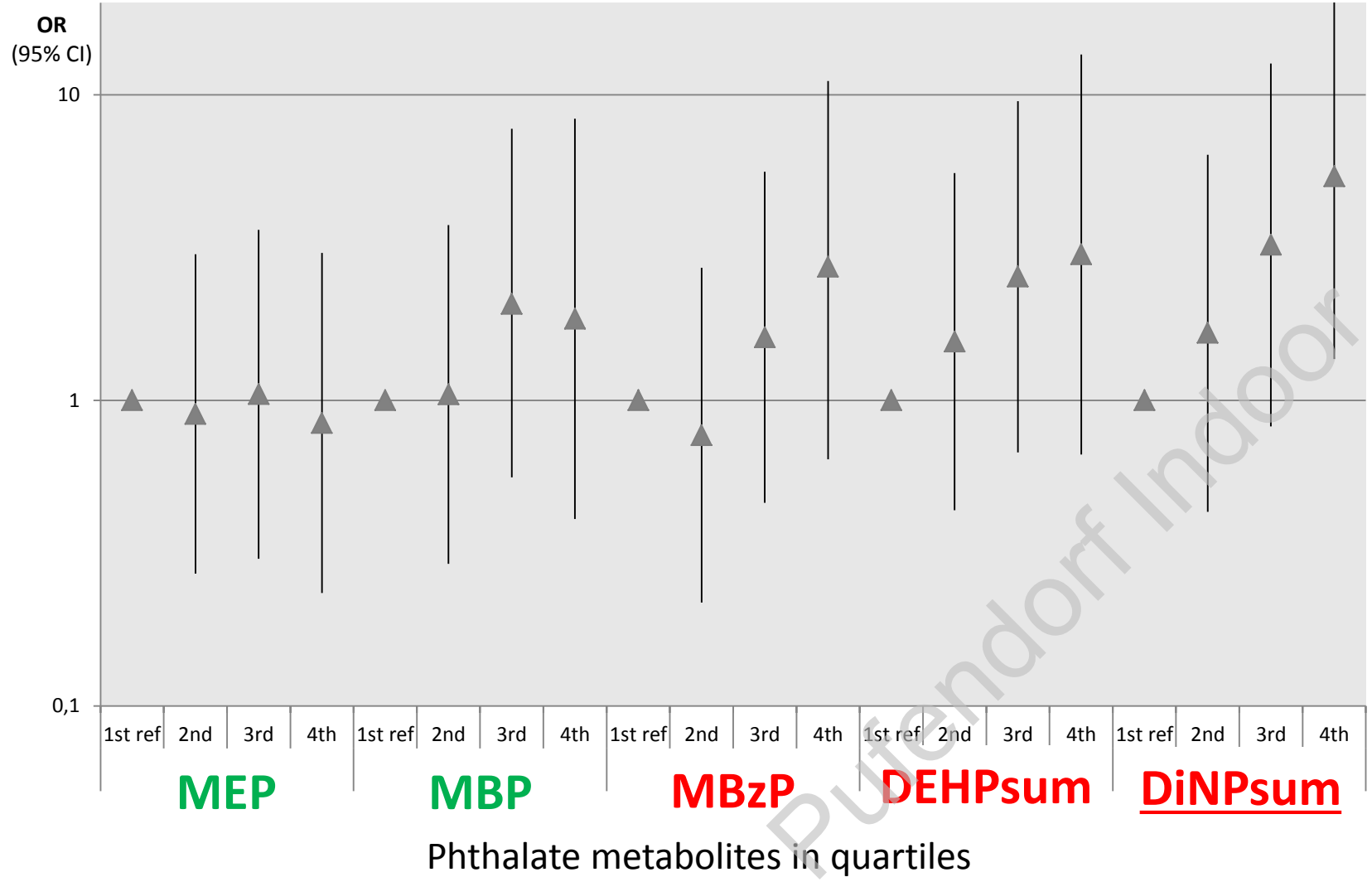
Prenatal Phthalate Exposures and Anogenital Distance in Swedish Boys

Carl-Gustaf Bornehag, Fredrik Carlstedt, Bo AG. Jönsson, Christian H. Lindh, Tina K. Jensen, Anna Bodin, Carin Jonsson, Staffan Janson, and Shanna H. Swan

http://dx.doi.org/10.1289/ehp.1408163

Received: 22 January 2014
Accepted: 10 October 2014
Advance Publication: 29 October 2014

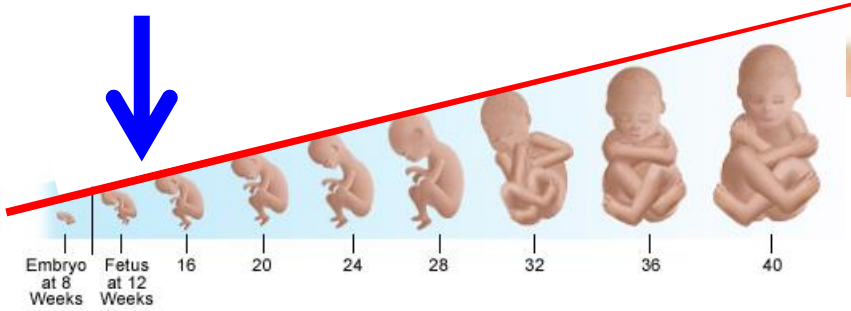
1st trimester DiNP exposure increase the risk for shorter AGD in 196 SELMA boys (21m)



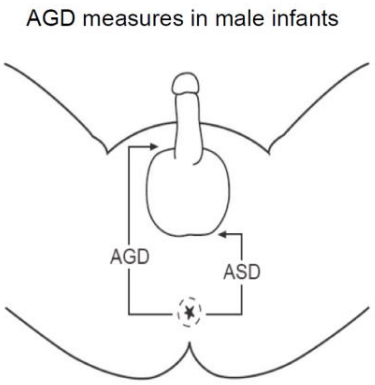
Natural sexual hormones

Estrogen

Testosterone



Sexual development & fertility



Chemicals with endocrine disrupting properties “Xenoestrogens”

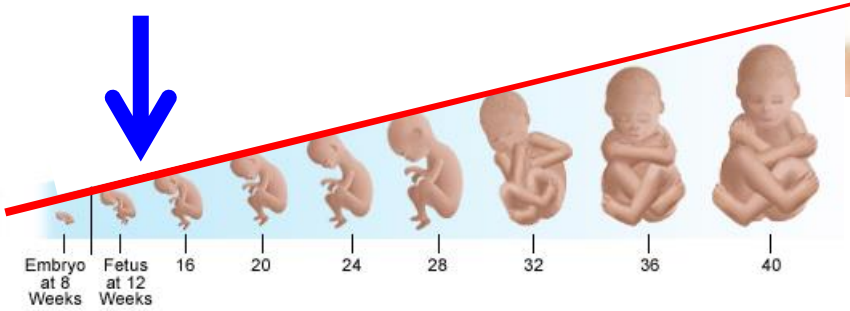
→ A shorter AGD

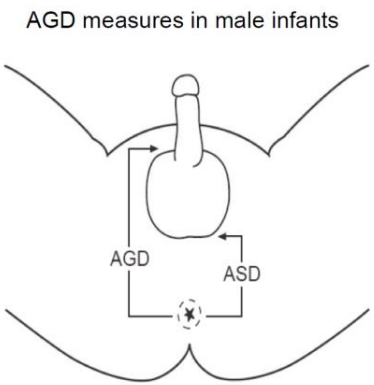
Incomplete masculinization

Natural sexual hormones

Estrogen
Testosterone

Sexual development & fertility





Chemicals with endocrine disrupting properties "Xenoestrogens"

→ A shorter AGD

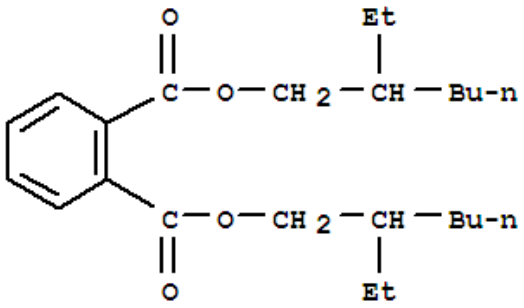
Newborn boys → Genital malformations

Adult men → Fertile problems

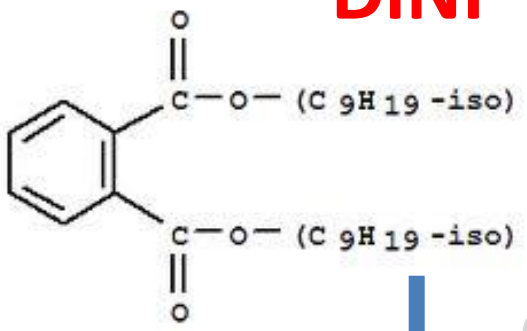
Examples of indoor related sources for DiNP

Replacement of phthalates in PVC

DEHP

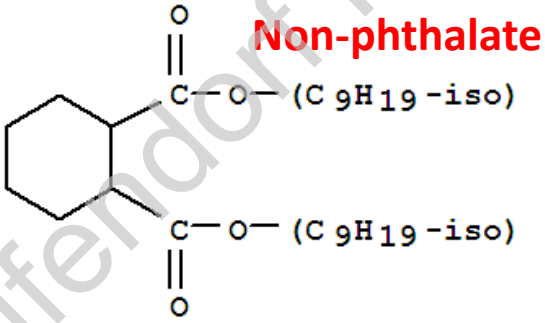


DiNP



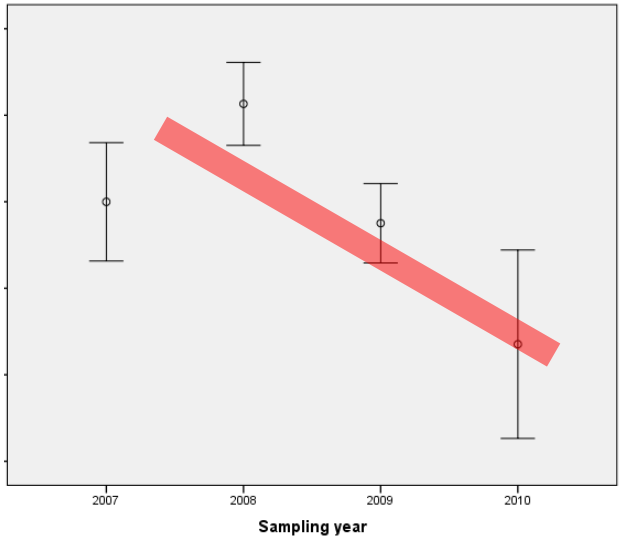
DINCH

Non-phthalate

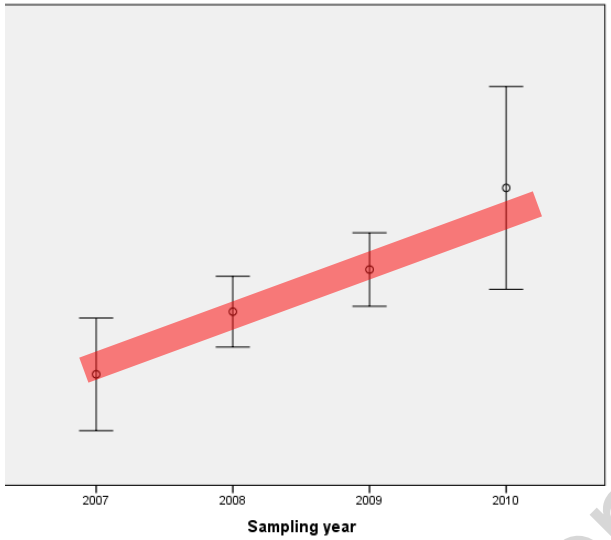


1st trimester urinary levels in 2,355 SELMA mothers

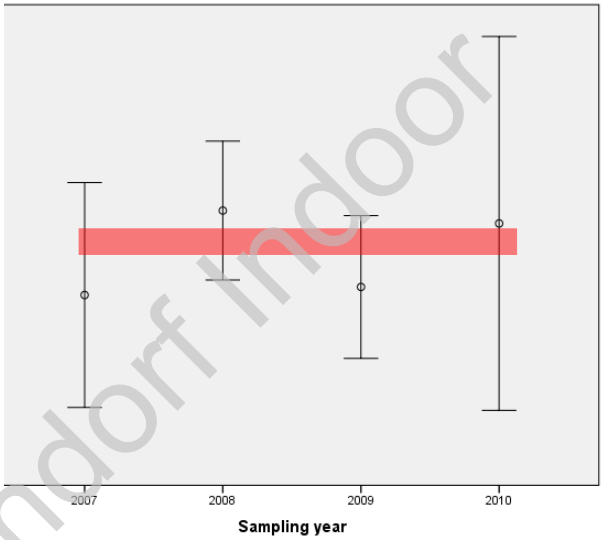
DEHP



DiNP



BBzP



KEMI
Kemikalieinspektionen

The four most used phthalates in Sweden 2012 (>1,000 ton/year)

- DPHP
- DEHP
- DIDP
- DiNP

Thank you!

Bornehag et al., 2004
Nilsson et al., 2005
Sundell et al., 2005
Bornehag et al., 2005
Larsson et al., 2009
Larsson et al., 2010
Choi et al., 2010
Choi et al., 2010
Guo et al., 2012
Carlstedt et al., 2013
von Kobyletzki et al., 2013
Kochback Bölling et al., 2013
Shu et al., 2014
Bornehag et al., 2014
Unenge Hallerbäck et al., *manuscript*
Von Kobyletzki et al., *manuscript*
Bohman et al., *manuscript*
Larsson et al., *manuscript*
Choi et al., *manuscript*
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