BPA and related chemicals: why worry?

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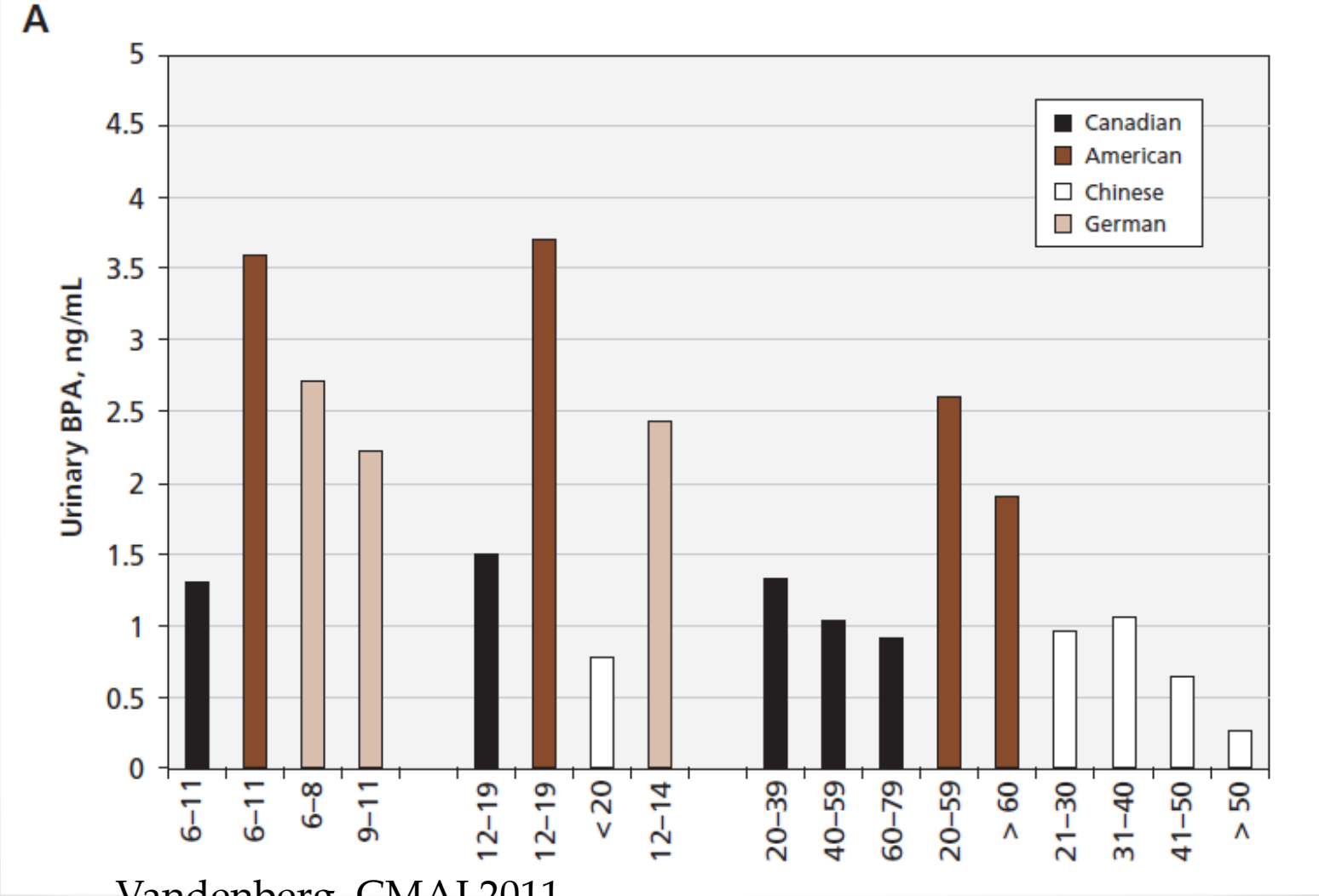
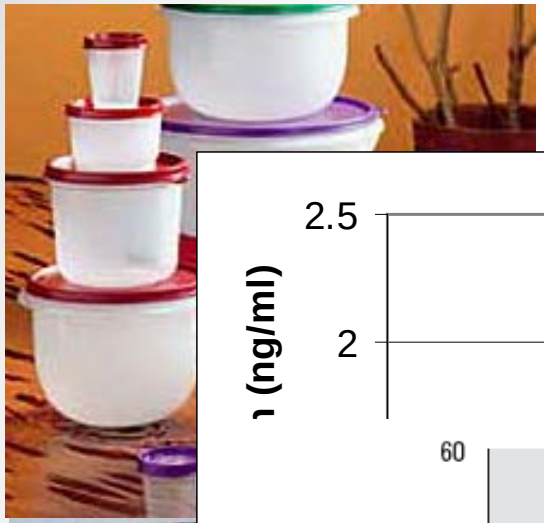
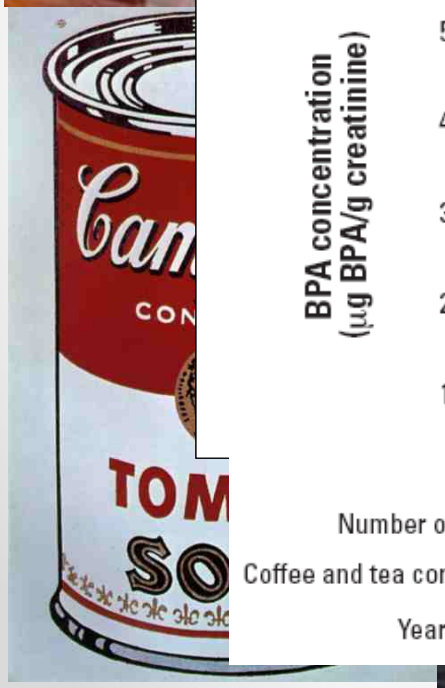
Human Exposures

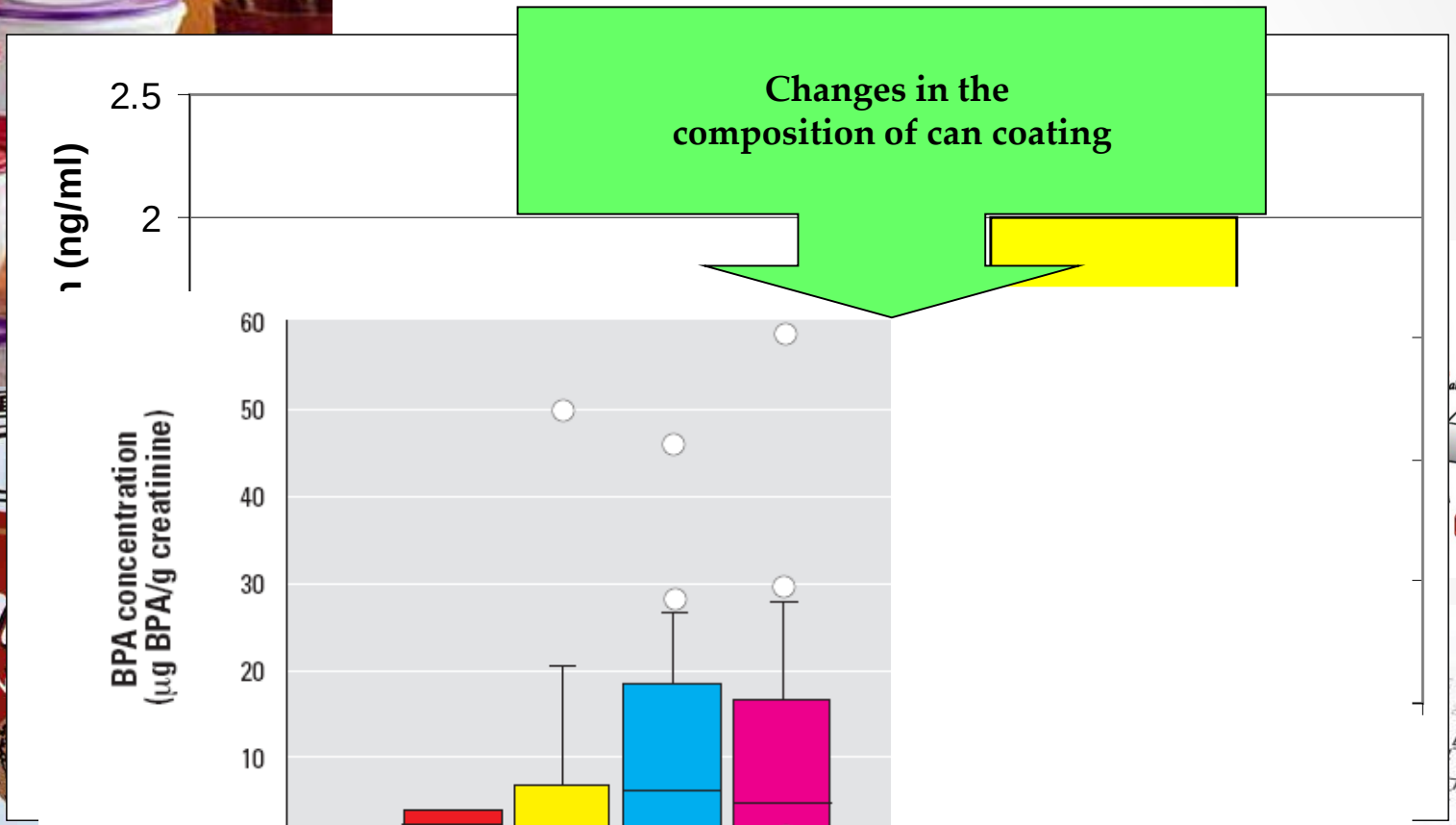


Vandenberg, CMAJ 2011

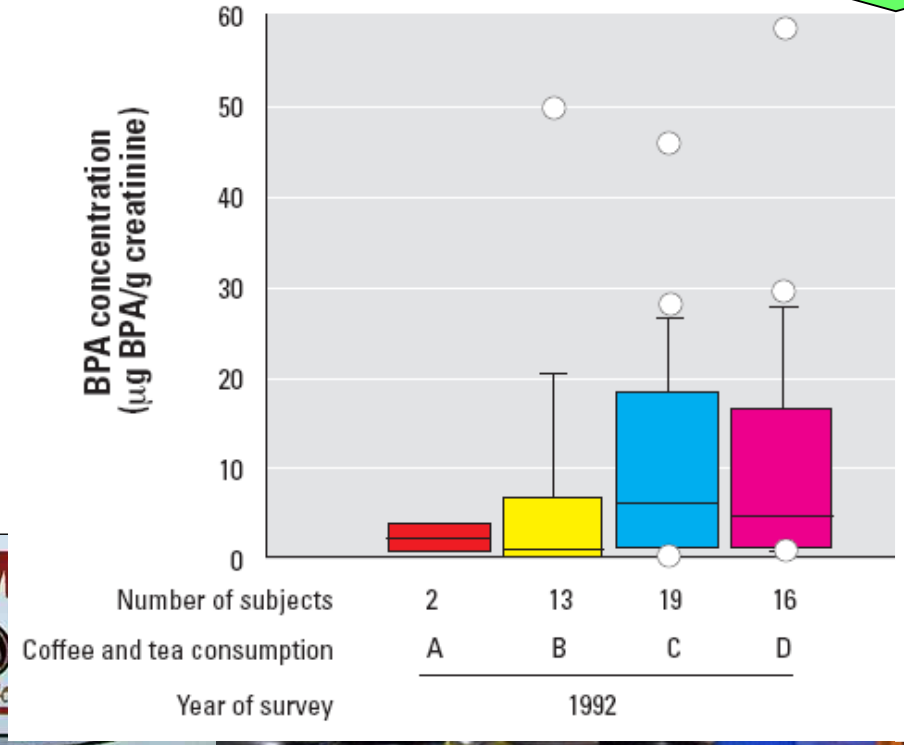
Sources of Exposure

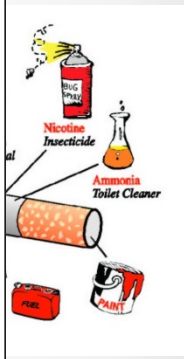


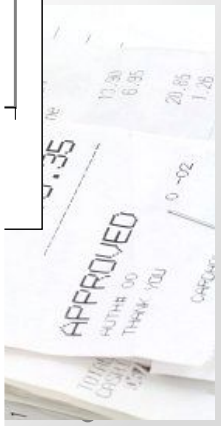




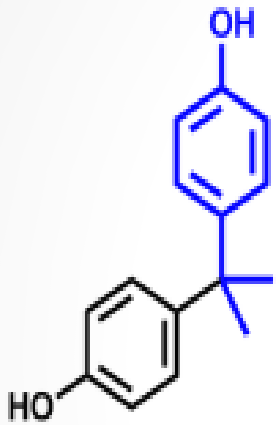
Changes in the composition of can coating



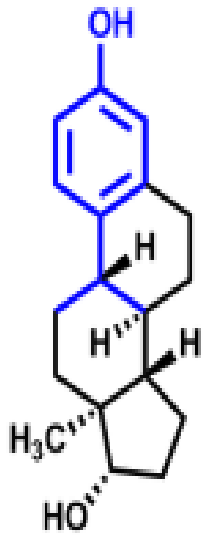




BPA is an endocrine disruptor

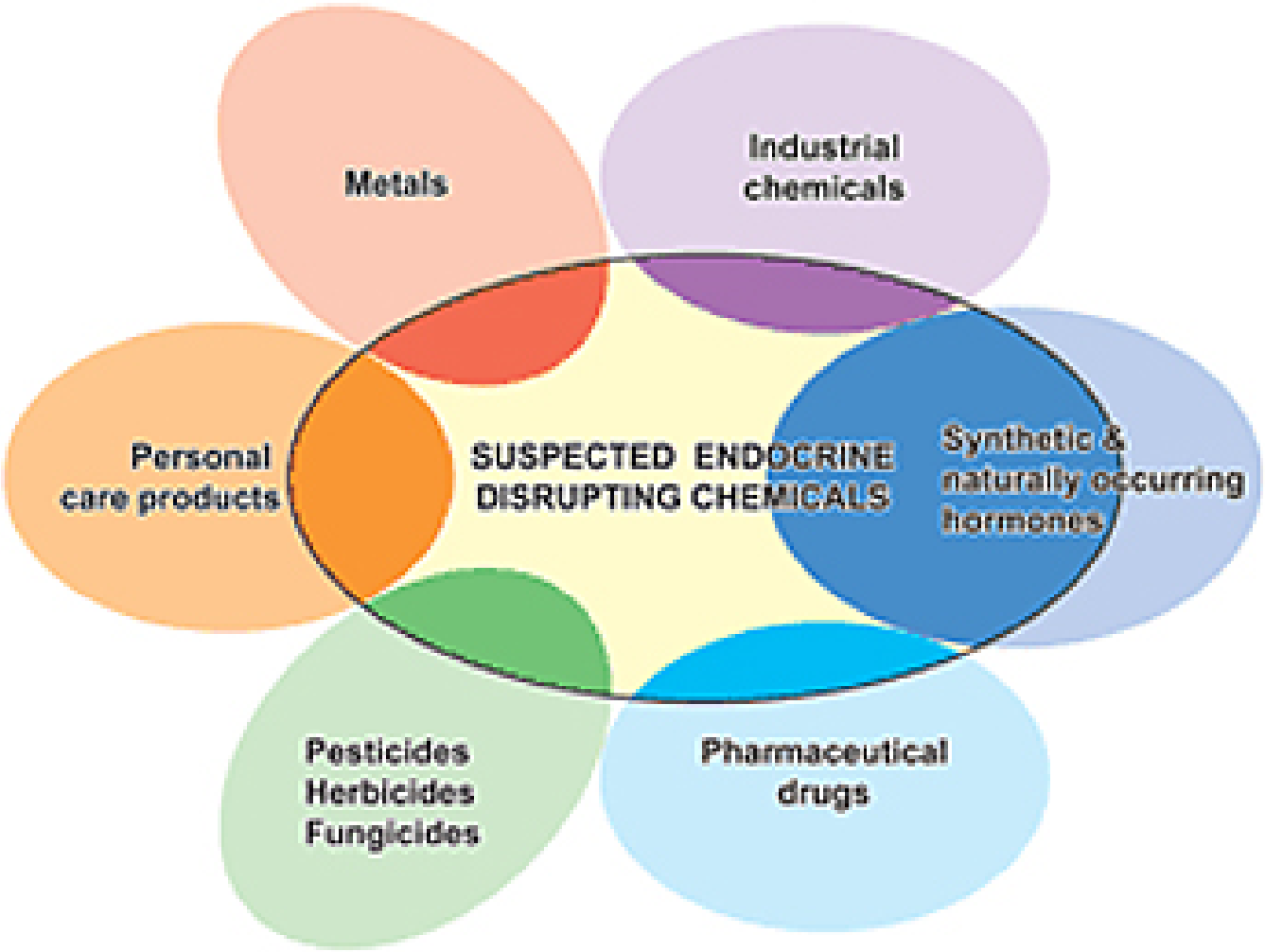


Bisphenol-A (BPA)



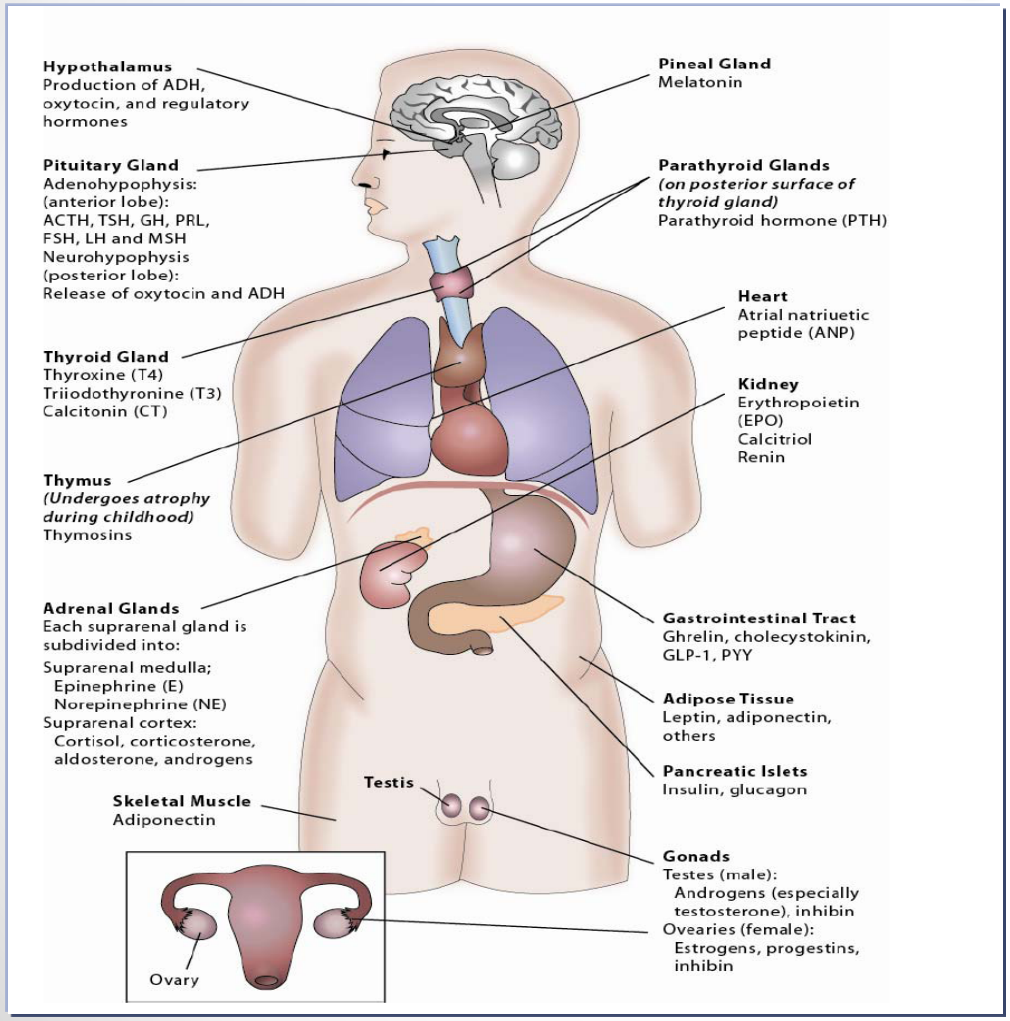
Estradiol

EDCs are exogenous chemicals or chemical mixtures that interfere in some way with hormone action.



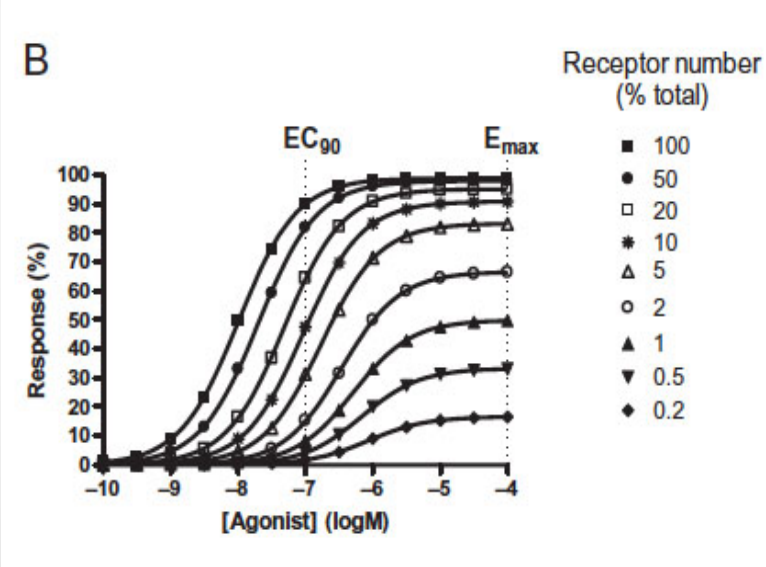
Some chemicals from the "families" above are potentially endocrine disrupters

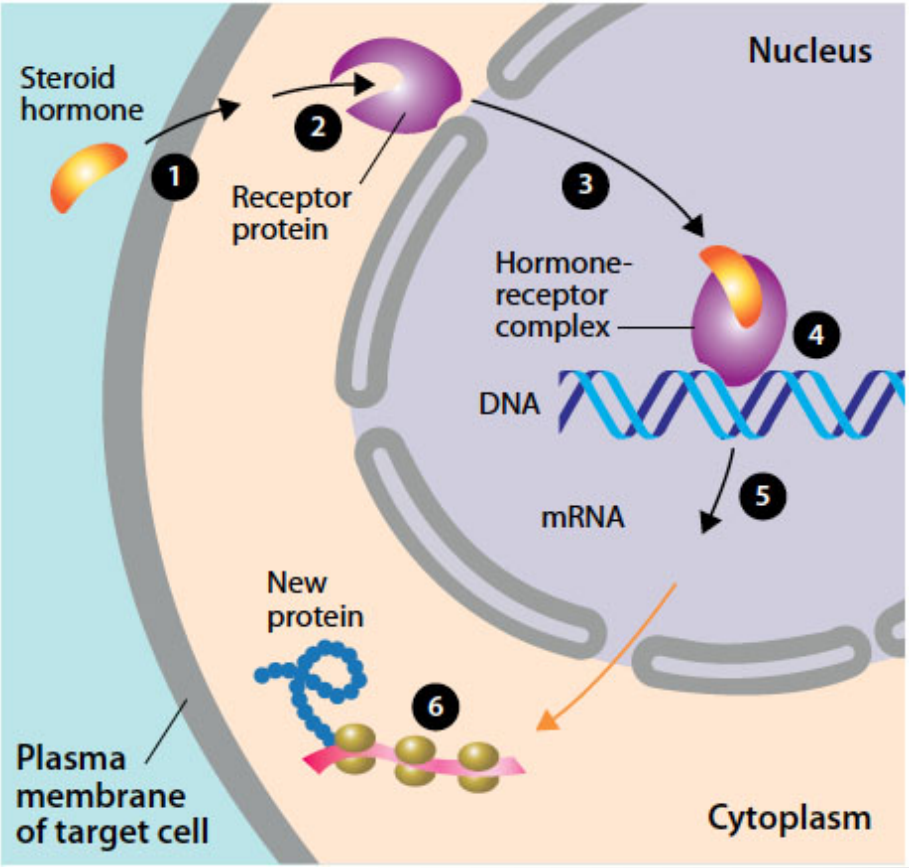
Understanding EDCs requires an understanding of hormones



Hormones act at low doses

Hormones act via receptors



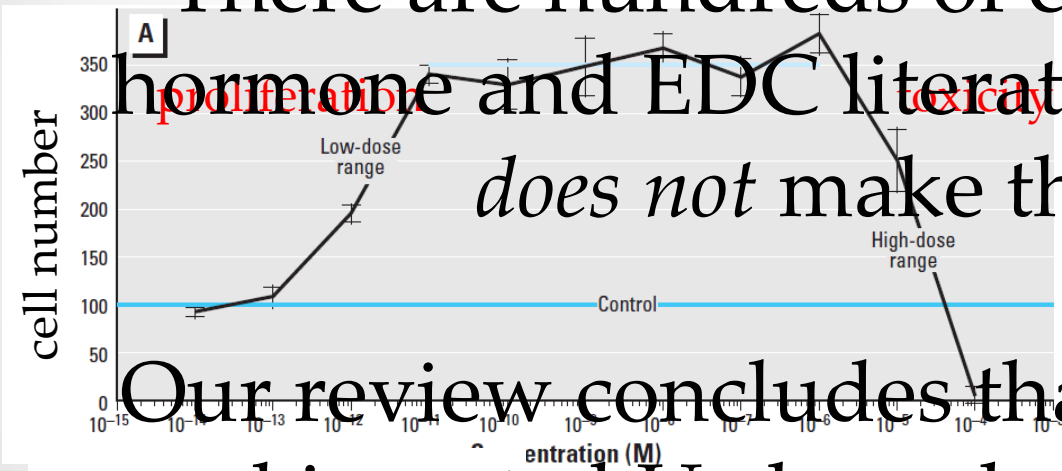


"potency" is endpoint specific

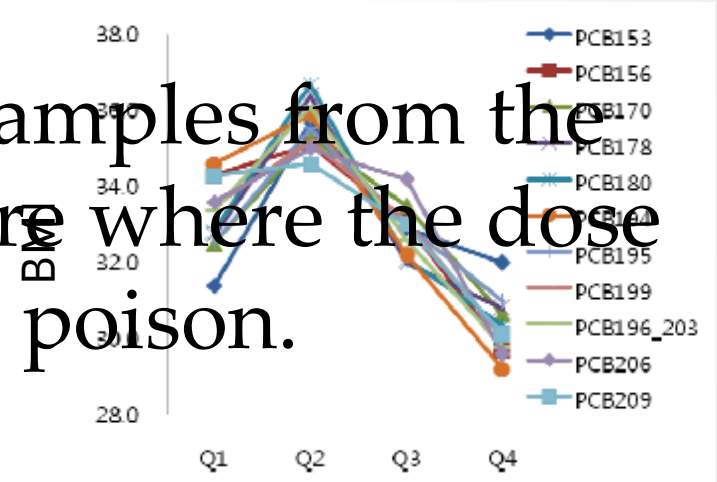
Hormones can have non-monotonic dose responses

There are hundreds of examples from the hormone and EDC literature where the dose *does not* make the poison.

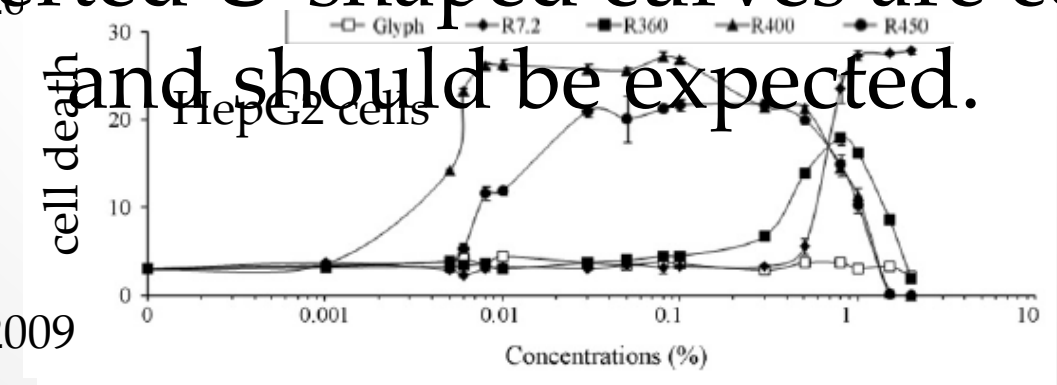
Our review concludes that these types of U- and inverted U-shaped curves are common and should be expected.



Weishons et al. 20



Lee et al. 2011



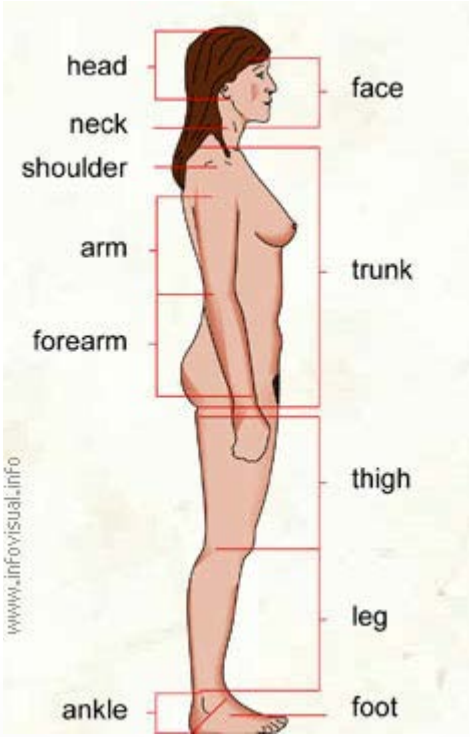
Gasnier et al. 2009

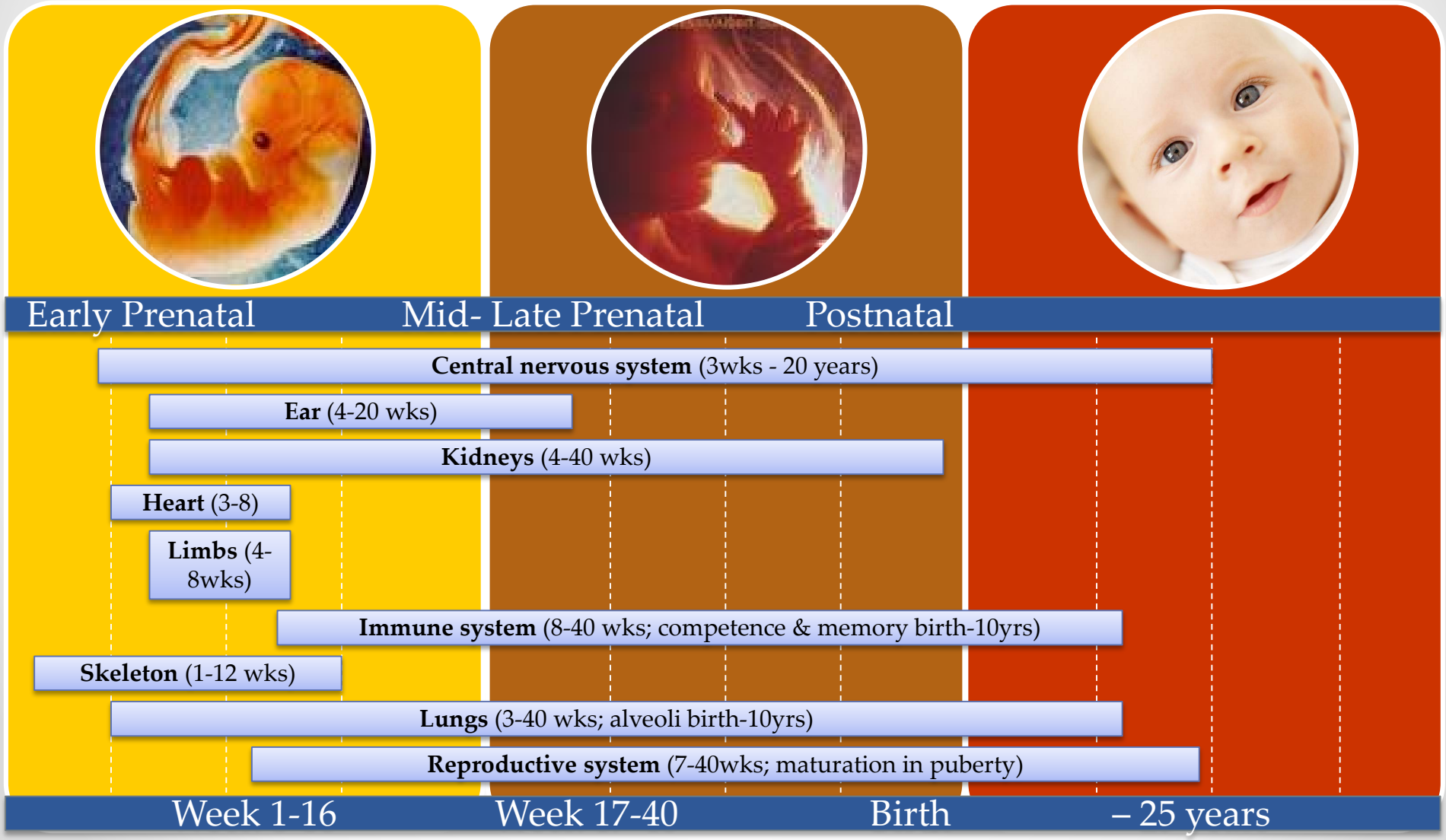
Hormone action is dependent on timing of exposure

"From the day of conception until an individual is born or hatched, the development of each stage of life is fully under the control of hormones.

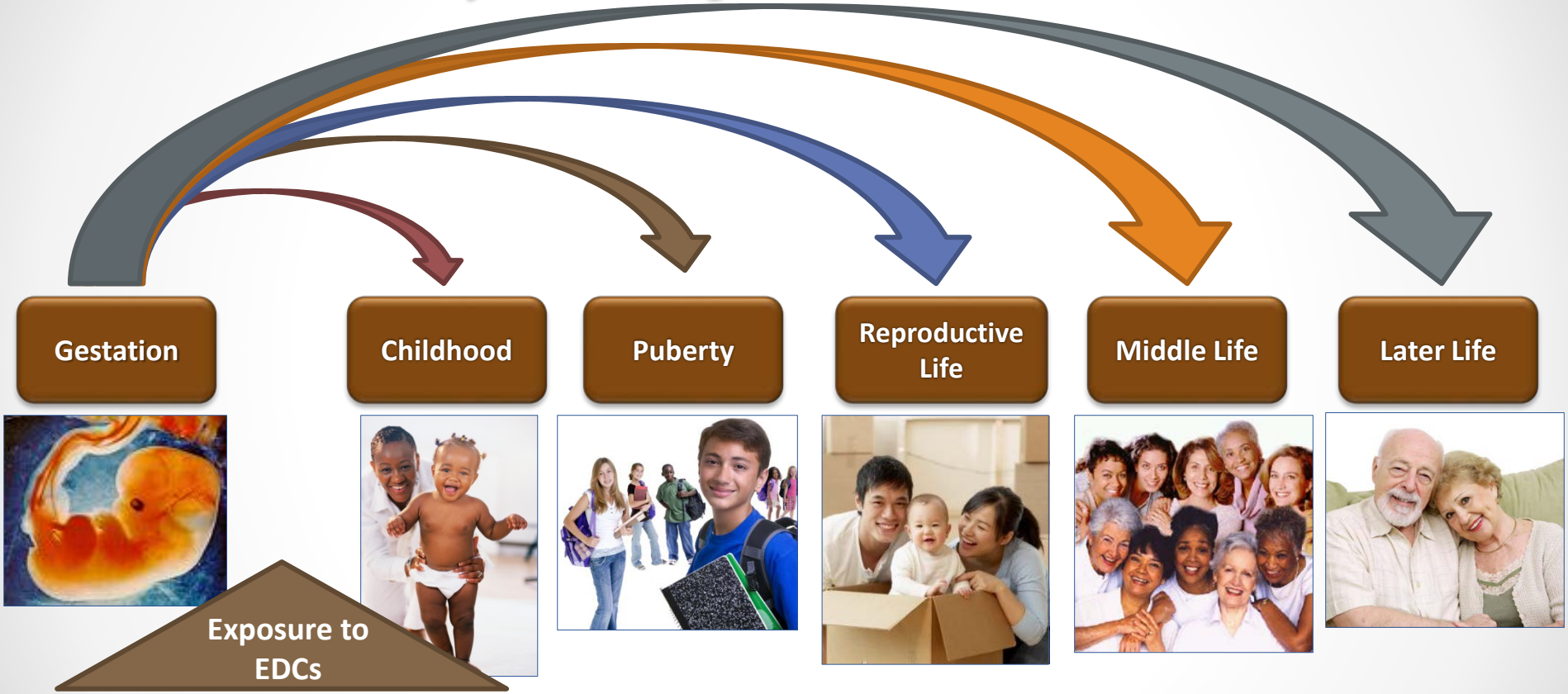
Changes that happen during development are far less reversible [than those occurring in an adult]; you can't go back and rewire the brain".

-Theo Colborn, zoologist, writer




Early Prenatal
Mid- Late Prenatal
Postnatal
Central nervous system (3wks - 20 years)
Ear (4-20 wks)
Kidneys (4-40 wks)
Heart (3-8)
Limbs (4-8wks)
Immune system (8-40 wks; competence & memory birth-10yrs)
Skeleton (1-12 wks)
Lungs (3-40 wks; alveoli birth-10yrs)
Reproductive system (7-40wks; maturation in puberty)
Week 1-16
Week 17-40
Birth
– 25 years

Early Life Exposure to EDCs

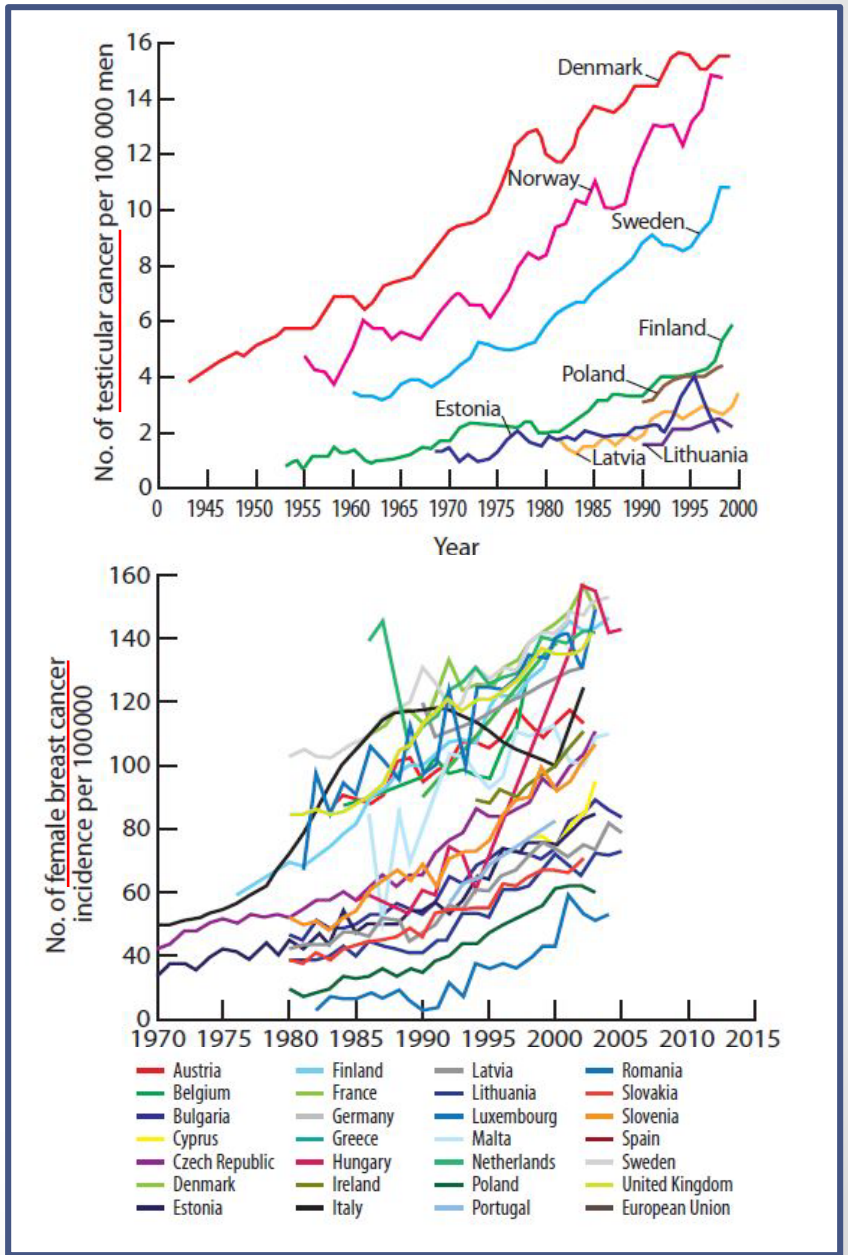


The effects of early exposures to EDCs – when organ systems are developing – may be manifested any time in life.

Human Disease Trends

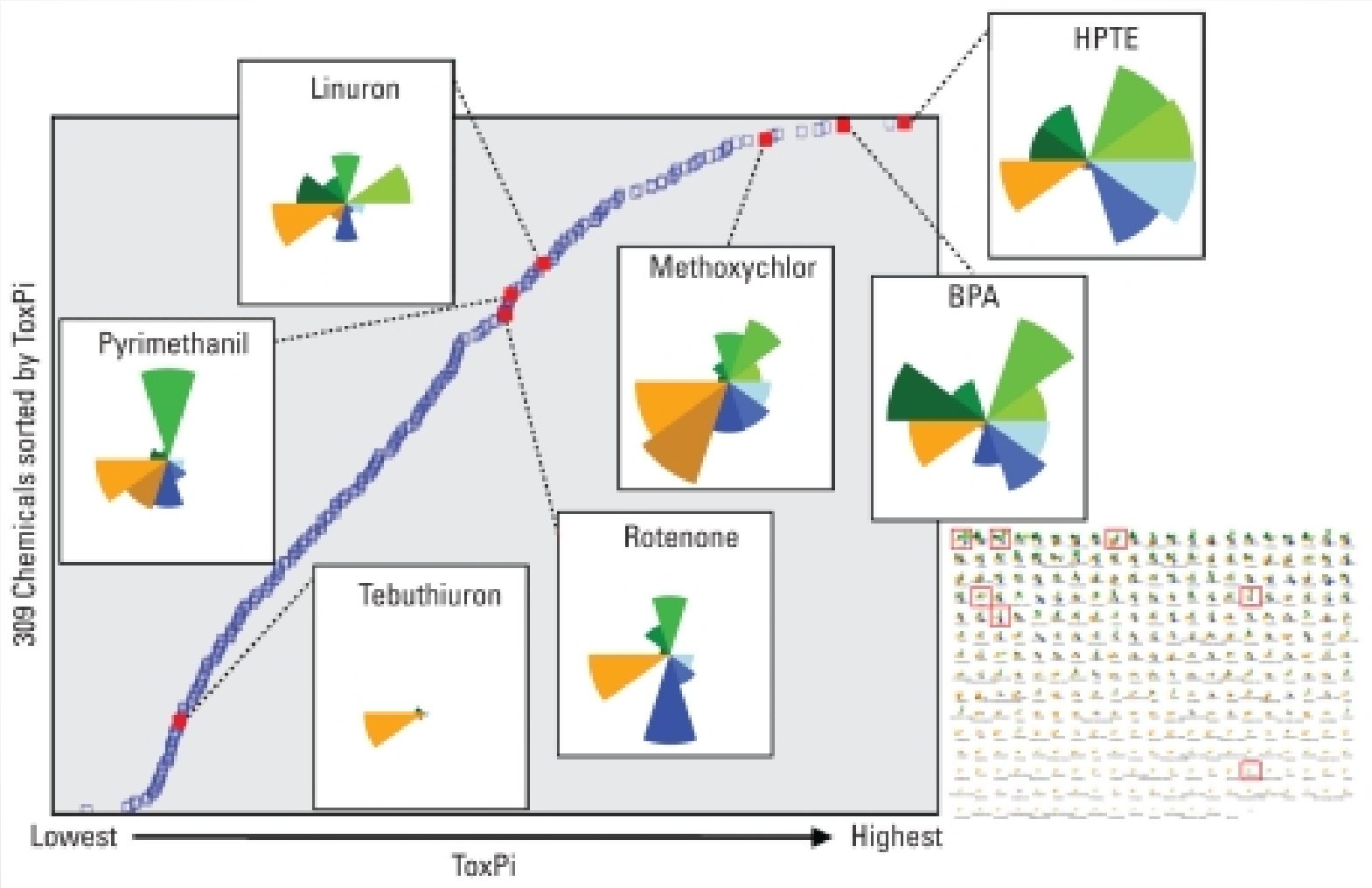
Over recent decades there has been:

- significant increase in **reproductive problems** in some regions of the world, suggesting a strong role for unidentified environmental factors in disease etiology
- increase in **endocrine cancers**
- significant decrease in **human fertility** rates
- increase in use of assisted reproductive services
- increasing number of chemicals to which all humans in industrialized areas are exposed



Top: Richiardi et al., Cancer Epidem. Biomark. (2004);
Bottom: based on data from http://data.euro.who.int/hfadb/

Back to BPA… What does it do?



Effects of BPA in animals

female reproductive tract

fertility

metabolic syndrome

immune system

cancers (prostate, mammary)

reproductive aging

hormone levels

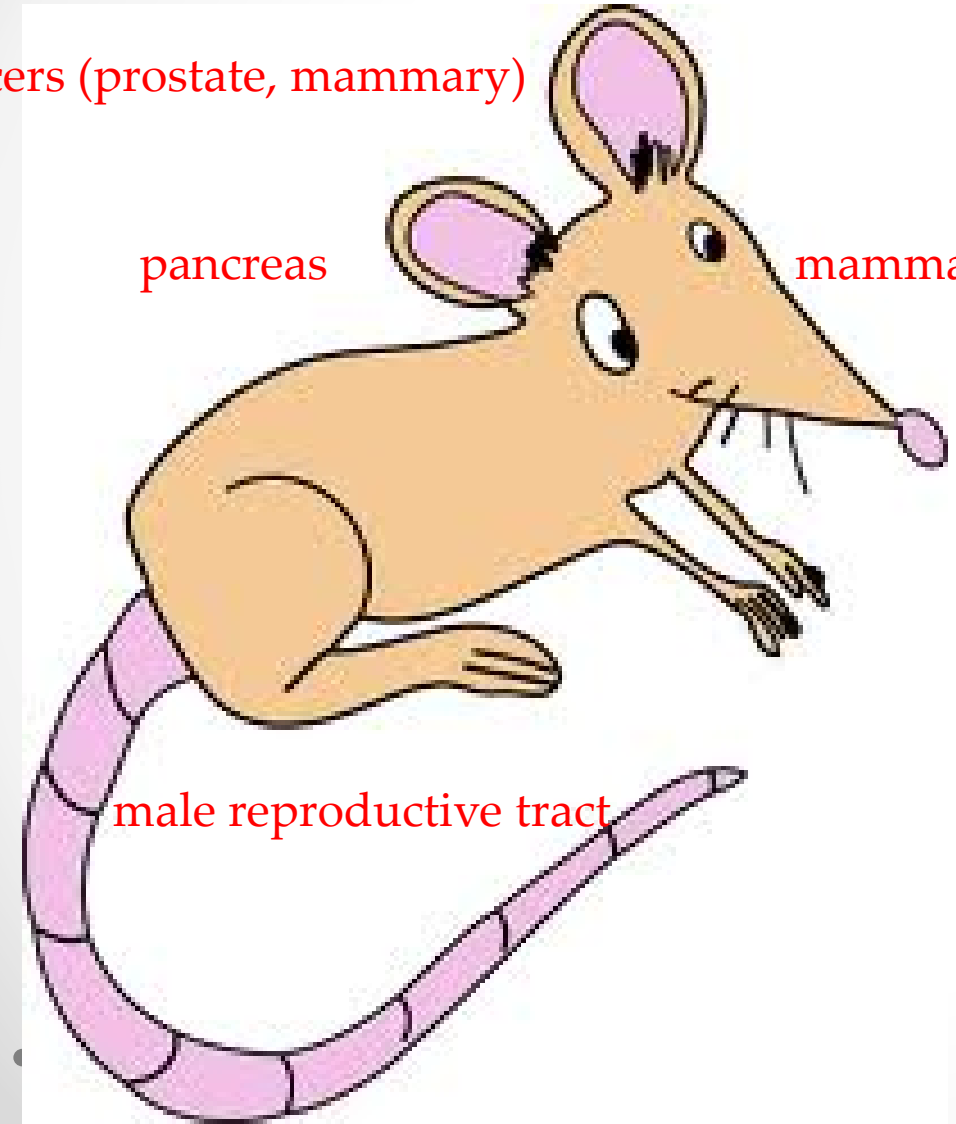
brain

pancreas

mammary gland

Behaviors (sex specific, maternal, aggression, hyperactivity)

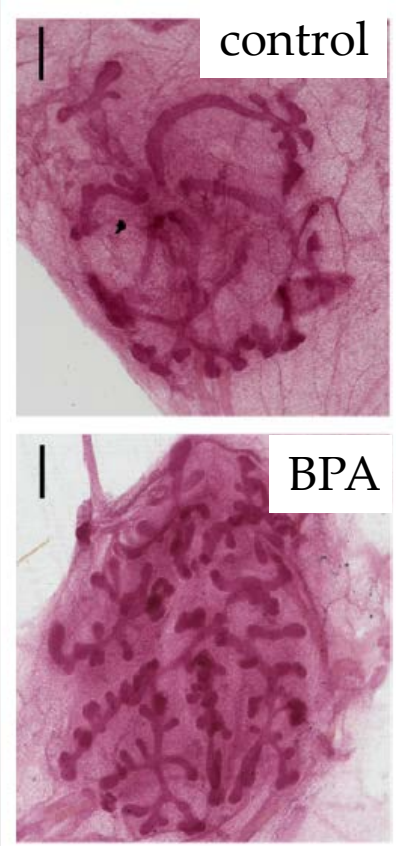
cardiovascular



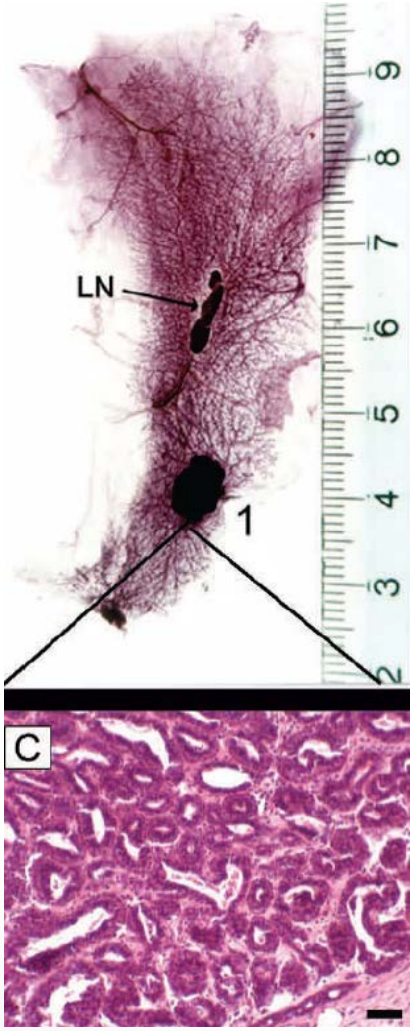
obesity

male reproductive tract

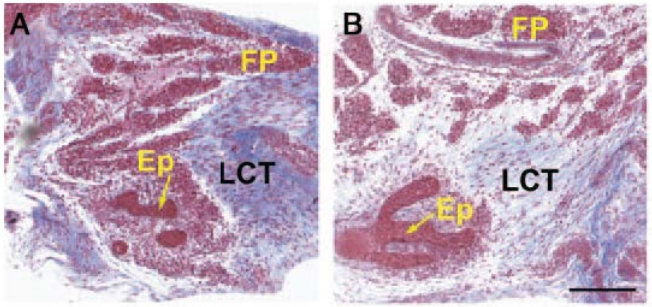
BPA & the mammary gland



Tharp et al. 2012

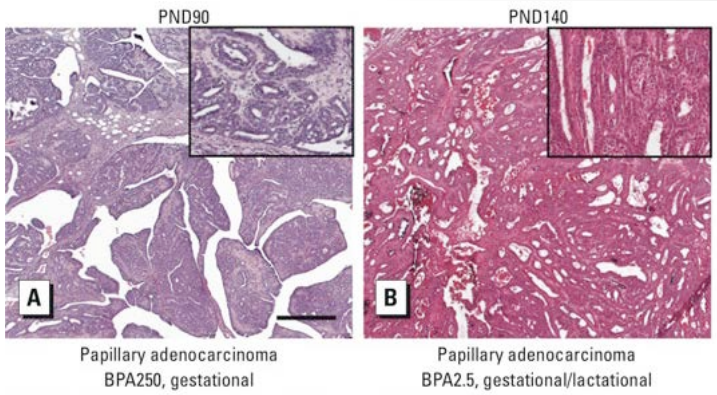


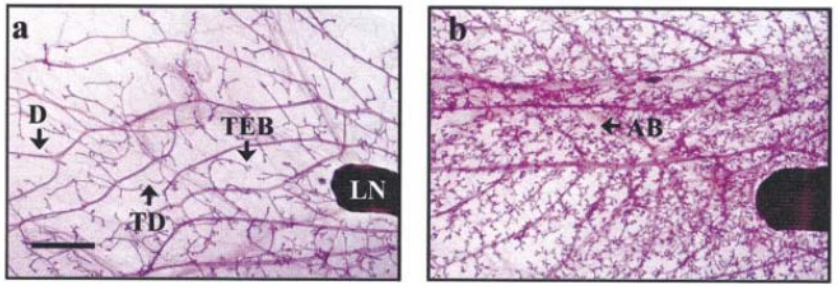
Durando et al. 2007



Vandenberg et al. 2007

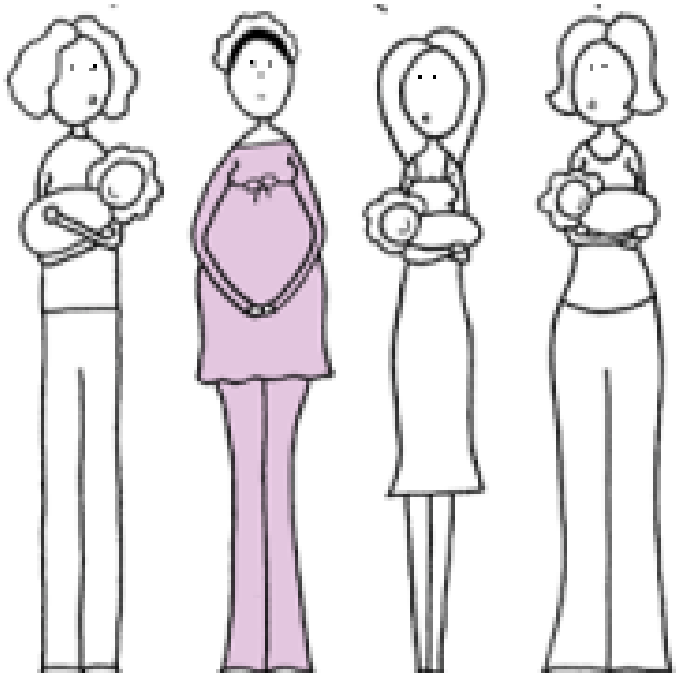
Acevedo et al. 2013





Markey et al. 2001

Effects of BPA in humans



PCOS

obesity

infertility

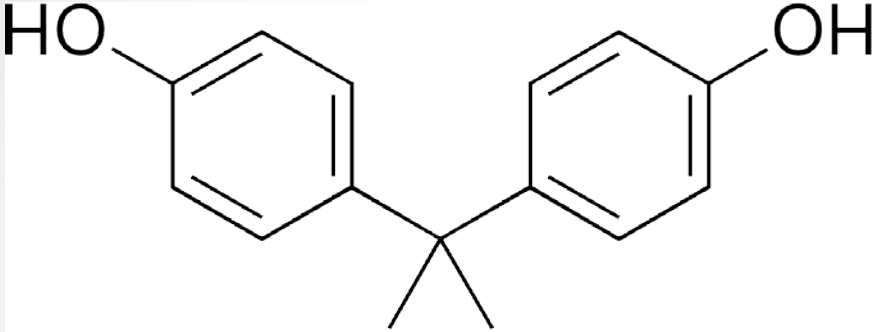
abnormal behaviors

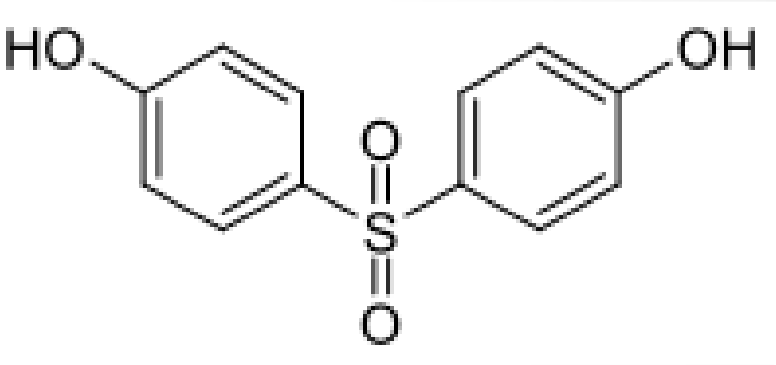
hormone levels

cardiovascular diseases

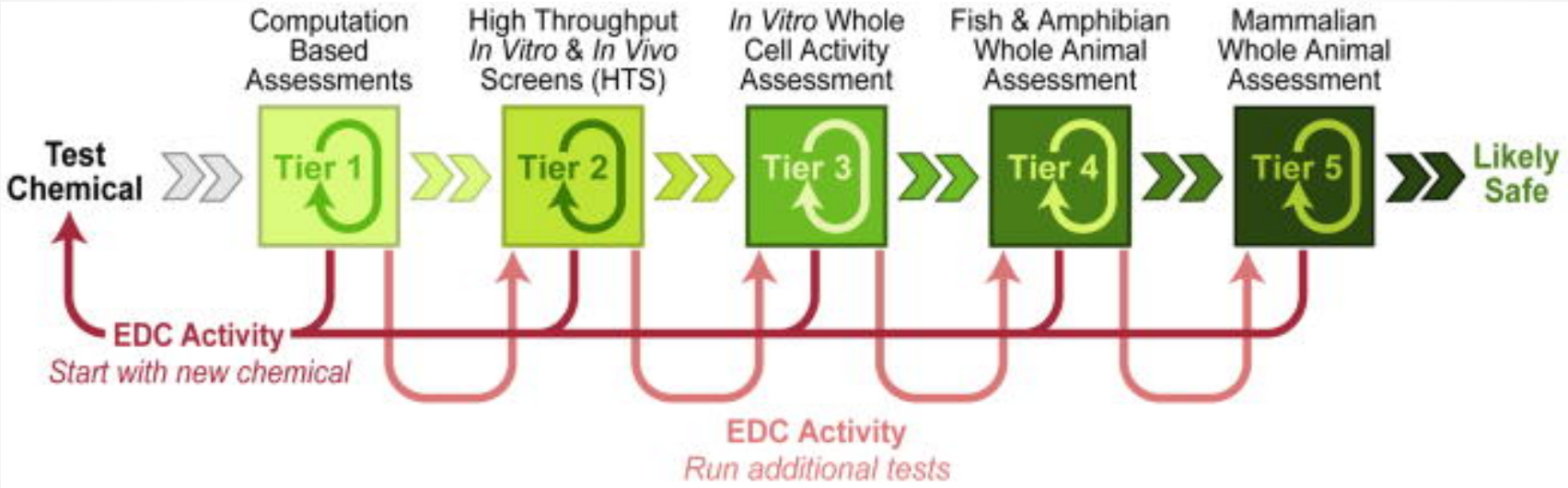
metabolic syndrome

BPA replacements





Changing how we test EDCs?



- Without appropriate testing, 'safety' should not be assumed
- 'positive' effects should trigger chemical abandonment