

Endocrine disruption and human health: Are there opportunities to prevent disease?

**John Peterson Myers, Ph.D.
Environmental Health Sciences**

**www.EnvironmentalHealthNews.org
www.OurStolenFuture.org**



Environmental Health Sciences

What do we know for certain?

Very little. Science yields certainty very cautiously.

Human epidemiology **doesn't prove** causation.

Animal experiments are **highly relevant**, but have not been carried out with humans.

It took decades to prove and accept tobacco causes lung cancer. This is **more complicated.**



Where is the evidence strongest?

High doses of EDCs cause

Infertility: DBCP, DES, Dioxins/PCBs

Cancers: DES, PCBs/dioxins, Vinyl chloride; Solvents, Some pesticides

Immune system disorders: Dioxins/PCBs

But often we don't know the mechanism.



Where is the evidence strongest?

Environmental doses of EDCs associated repeatedly with:

Impaired cognitive development: PCBs

Infertility: Some pesticides, phthalates

Immune system disorders: Dioxins/PCBs

Some cancers: Non-hodgkin's lymphoma, childhood leukemia

Type II diabetes: POPs



Diabetes risk and POPs?

Diabetes risk:
NHANES data
2,016 subjects

6 POPs:

PCB153 0.001

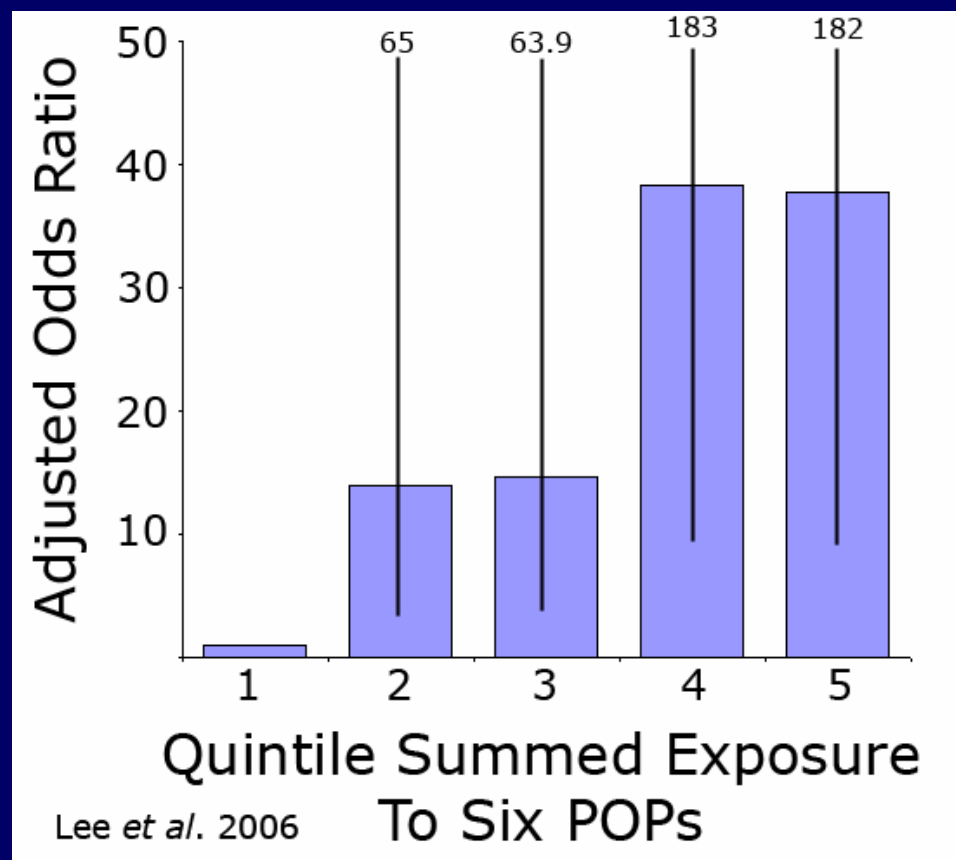
Heptadioxin 0.007

OCDdioxin 0.094

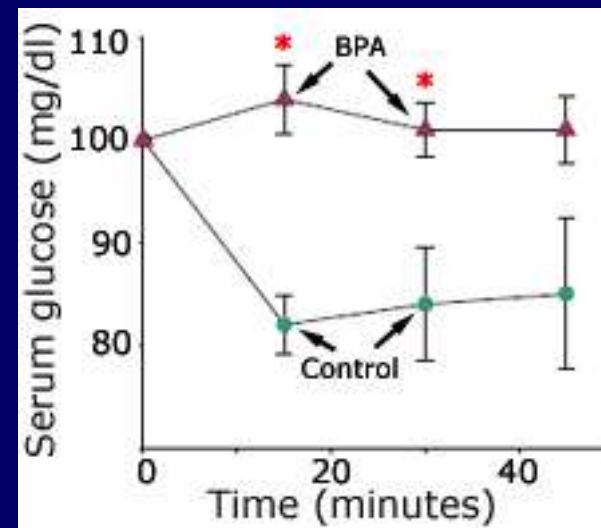
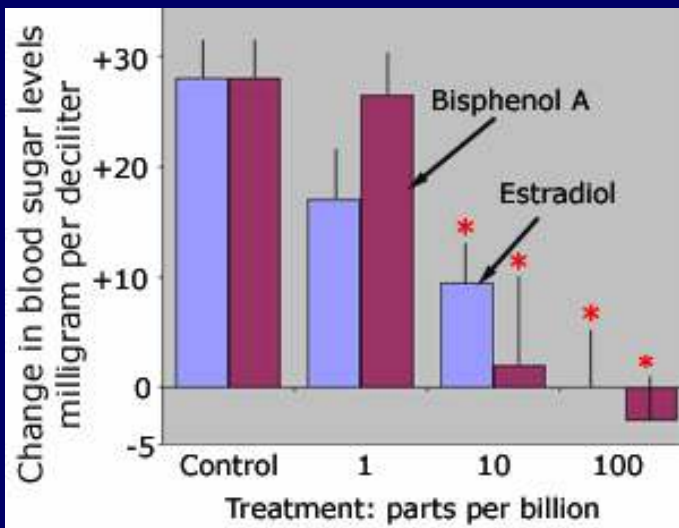
Oxychlorane 0.001

DDE 0.001

trans-Nonachlor 0.001



Bisphenol A causes insulin resistance in mice



Rapid response:
30 min after addition of
BPA or estradiol:
Blood sugar drops because
insulin increased

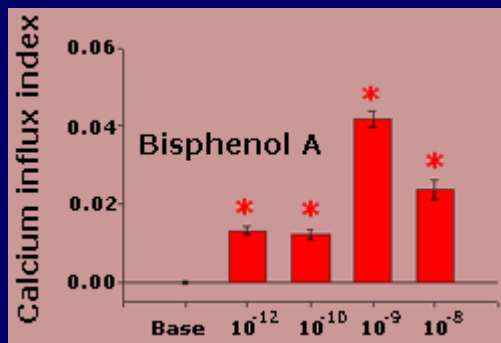
Slower response:
After 4 days BPA-treated
animals no longer
respond to insulin



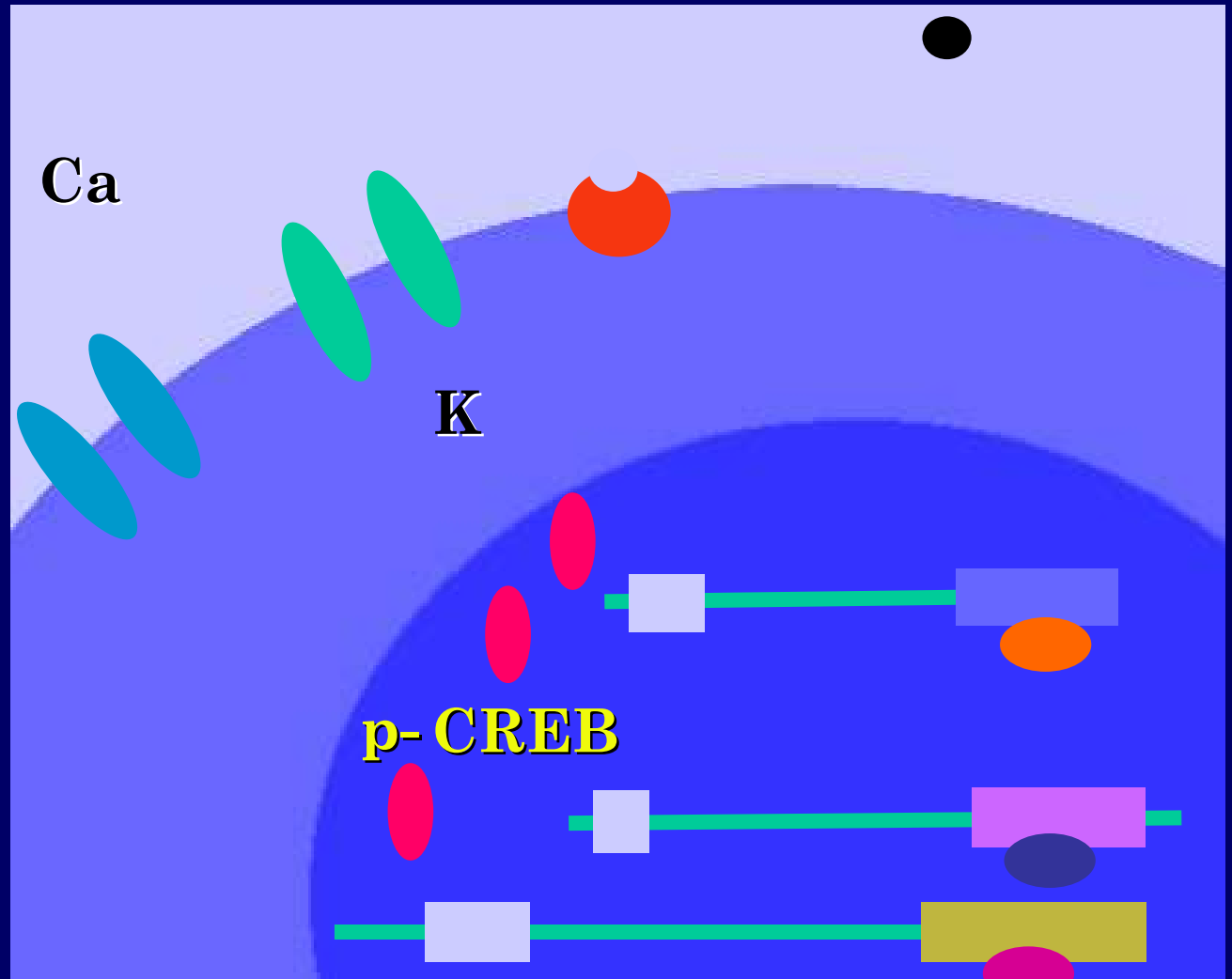
Bisphenol A at 'everyday levels'



Wozniak et al. 2005



95% of Americans



Quesada et al. 2003



Link to obesity?



1 part per billion DES
in the womb

Newbold *et al.* 2005

Same strain of mice
Same caloric intake
Same activity levels

The difference?



A scientific challenge

Toxicology as it has been practiced for decades is highly likely to have **underestimated hazards.**

Human epidemiology as it is been traditionally practiced is highly biased toward **false negatives.**

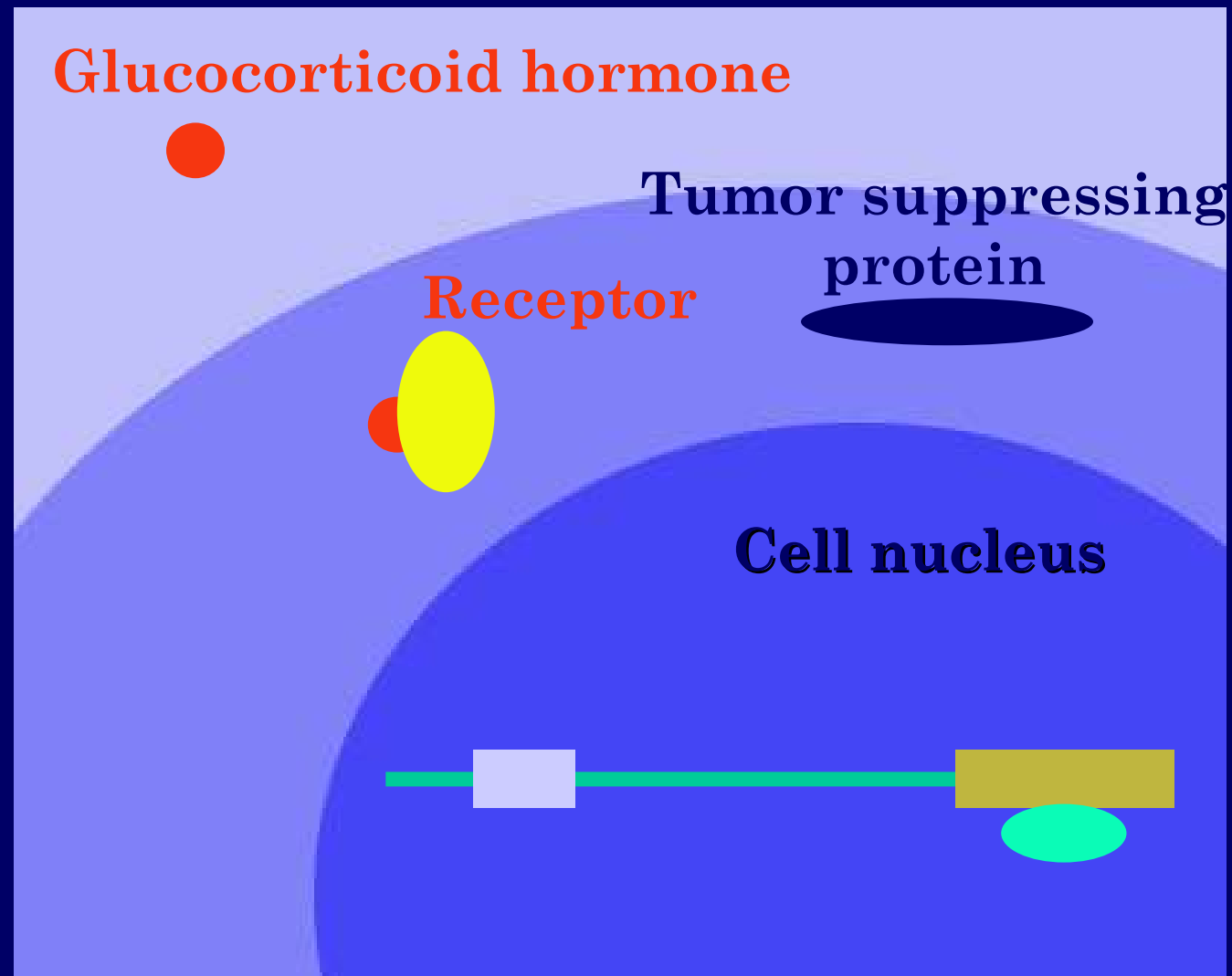


Four key scientific discoveries

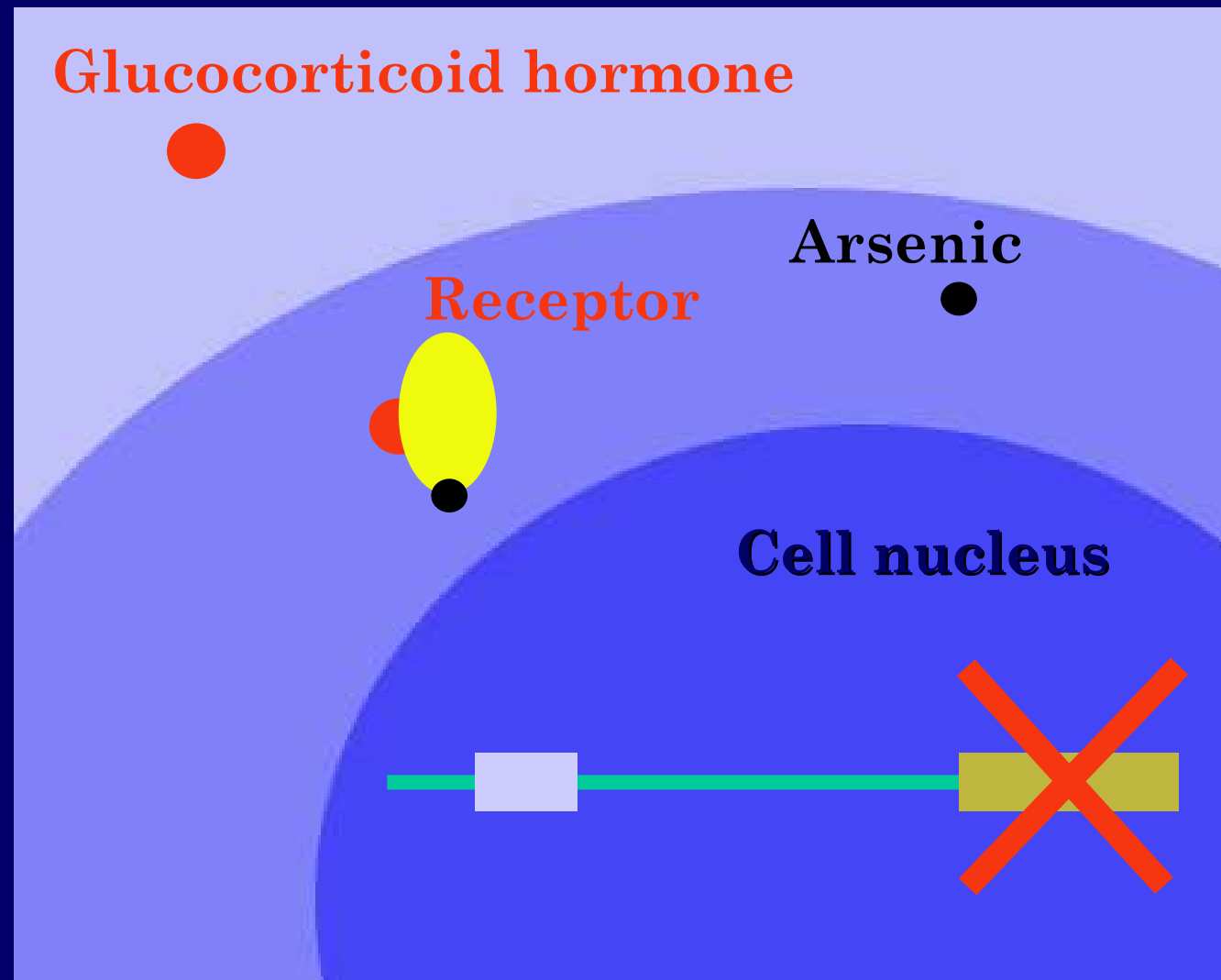
- Some contaminants can alter gene behavior at **extremely low doses**.
- Adult diseases and sensitivity to subsequent exposures can be **programmed during development**.
- High dose experiments don't predict those **low dose impacts**.
- Mixtures are ubiquitous; they alter impacts, sometimes **unpredictably**



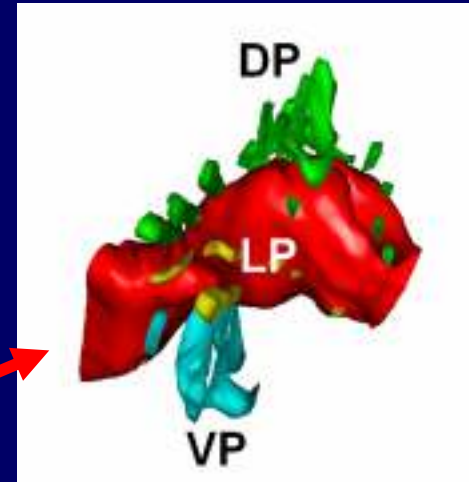
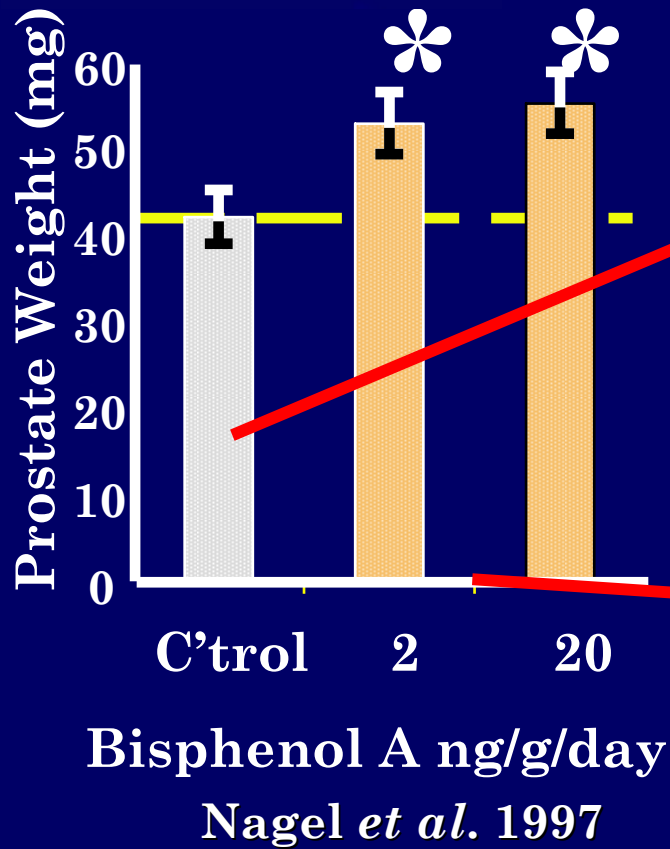
Low levels matter: Arsenic



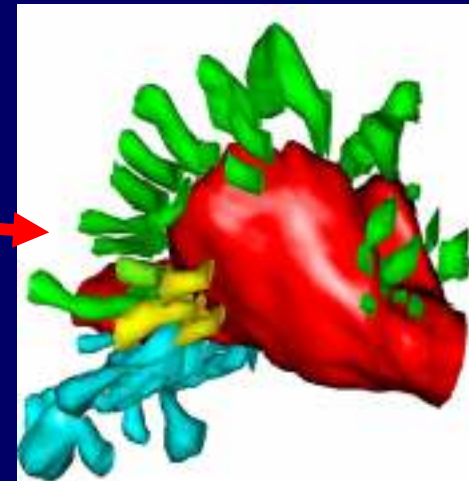
Low levels matter: Arsenic



Low doses matter



Timms *et al.* 2005

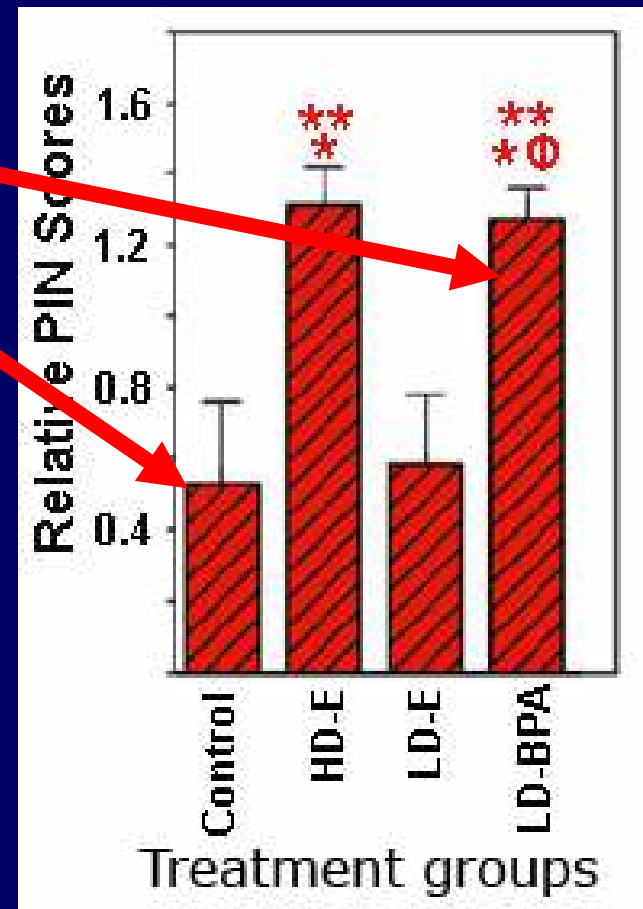


Low doses of bisphenol A



10 ppb BPA
compared to
control

Perinatal exposure to
10 ppb causes adult
prostate cancer
(prostatic epithelial neoplasias)
by altering adult gene
expression.



Ho *et al.* 2006



Bisphenol A : Many studies showing impact at low levels

Through Nov. 2006: 161 animal studies of BPA at current human exposure levels



12 funded by industry

149 funded by gov't

	Effect	No effect
12 funded by industry	0	12
149 funded by gov't	138	11

Over 80 *in vitro* studies also show low dose effects.

Updated from Welshons *et al.* 2006

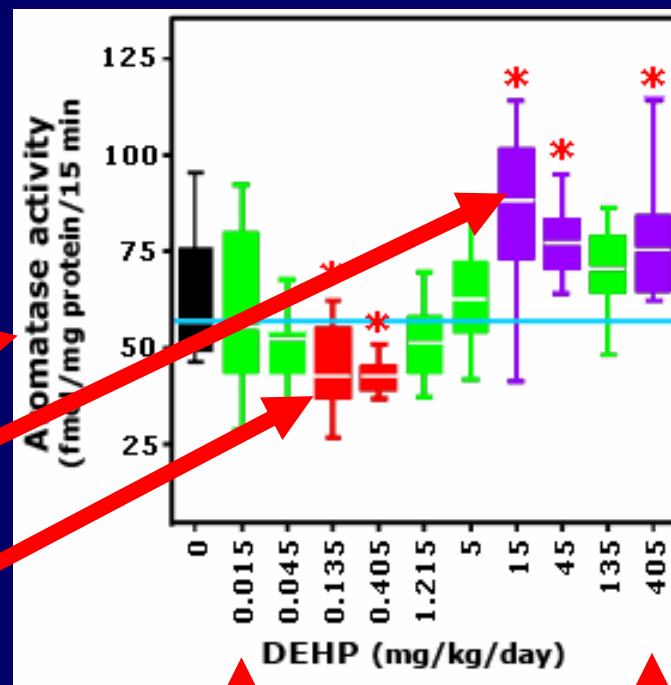


Does dose make the poison?

Exposed perinatally

Wide range of exposures

Brain enzyme measured once adult



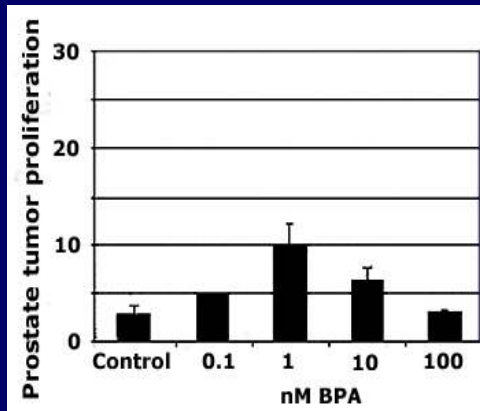
Andrade *et al.* 2006

High doses increase gene expression

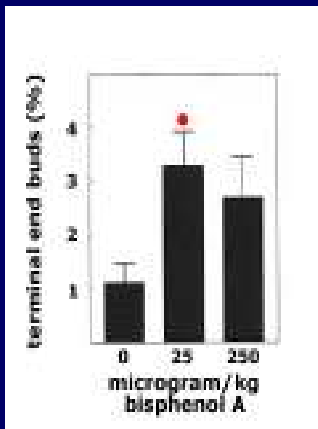
Low doses suppress gene expression 15 ppb 405 ppm



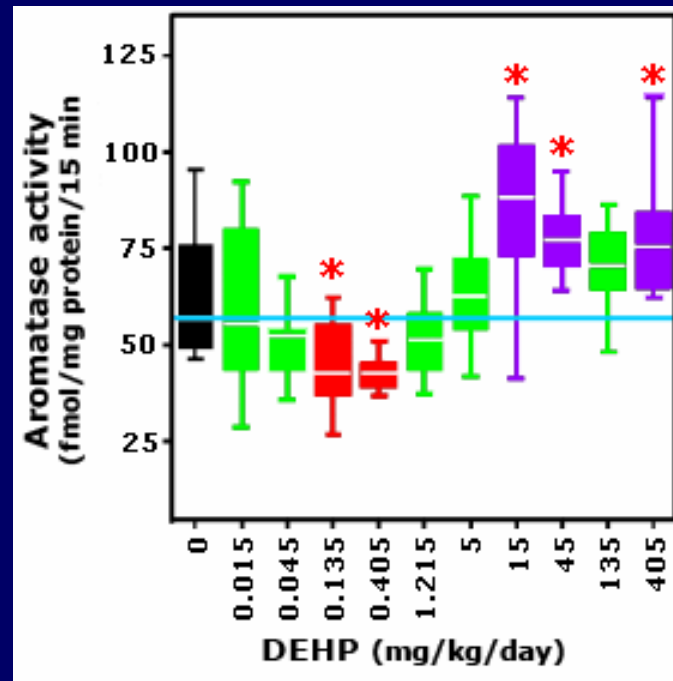
Does dose make the poison?



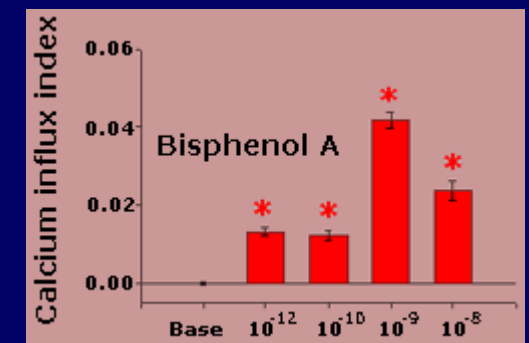
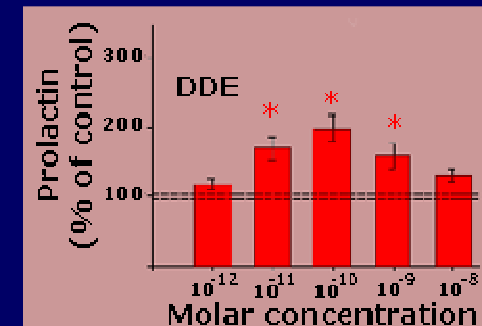
Wetherill *et al.* 2002



Markey *et al.* 2001



Andrade *et al.* 2006



Wozniak *et al.* 2005



Does dose make the poison?



Newbold *et al.* 2005

1 part per billion DES
in the womb

100 ppb causes
weight loss

Same strain of mice
Same caloric intake
Same activity levels

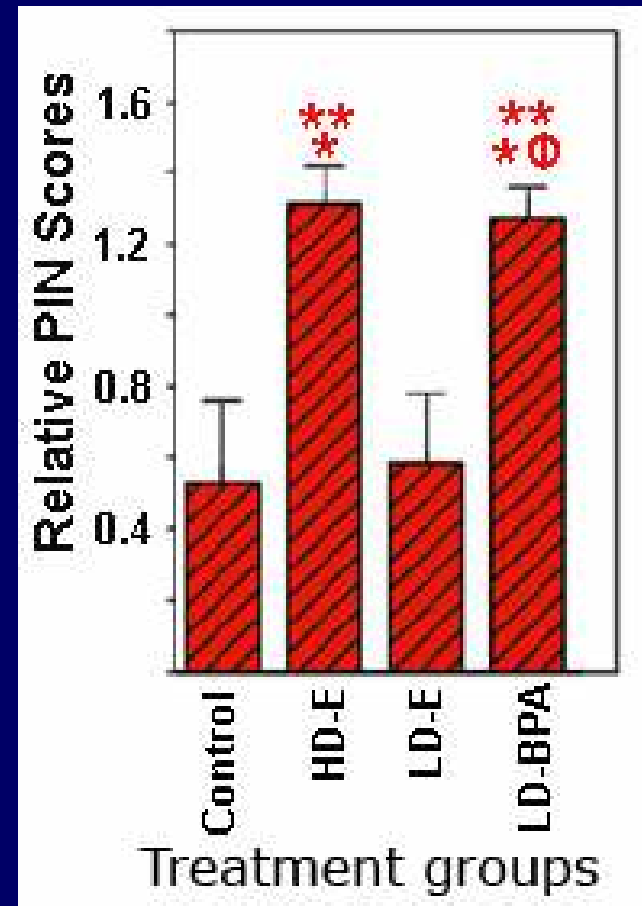
The difference?



Fetal programming => Adult disease



Perinatal exposure to 10 ppb causes adult prostate cancer (prostatic epithelial neoplasias) by altering *adult* gene expression.



Ho *et al.* 2006



Bisphenol A tied to prostate cancer in rats

Ho *et al.* 2006

PDE4D → Phosphodiesterase → cAMP ↓

Adult control animals

$\text{CH}_3 \text{ CH}_3 \text{ CH}_3$
PDE4D → Phosphodiesterase → cAMP

Adult BPA-exposed

PDE4D → Phosphodiesterase → cAMP



Fetal programming

=> Adult disease

Many animal experiments

**Cancers: Prostate, breast, testicular,
etc. (Reviewed by Birnbaum and Fenton)**

Infertility

**Neurocognitive impairments,
behavioral changes**



Fetal programming

=> Adult disease

What does this mean for epidemiology?

Long Island Breast Cancer study

New methods being developed

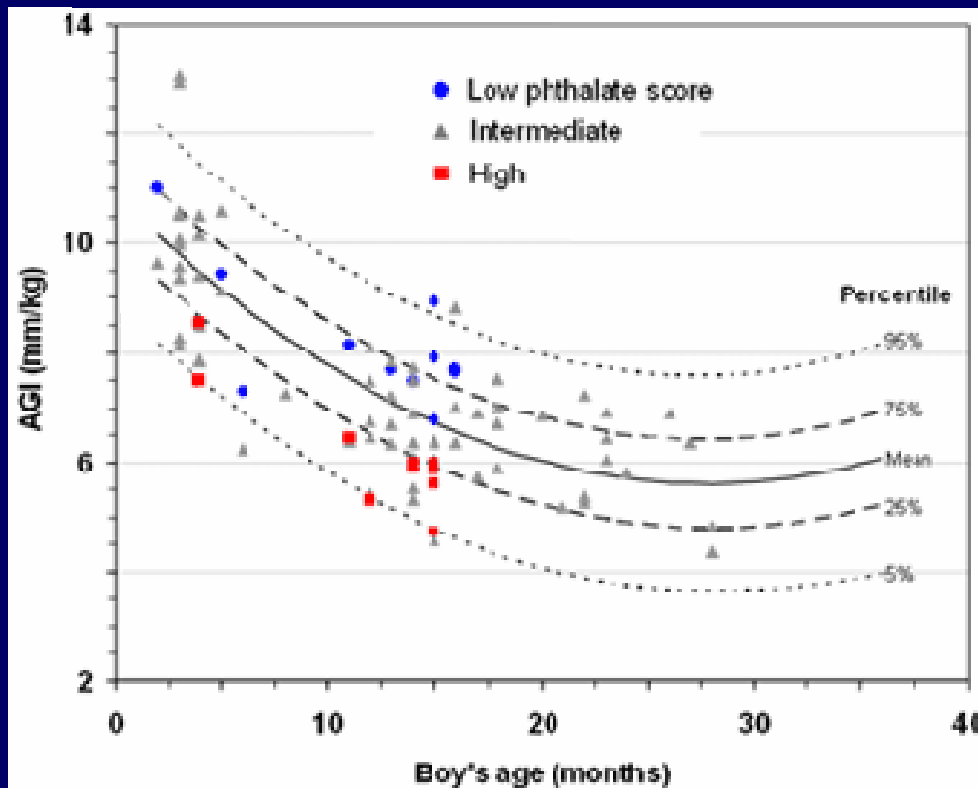
Stored tissues and fluids: Cohen,
Longnecker

Creative study design: Hardell

Design based on new toxicology: Swan



Epidemiology advances



Large risks associated with phthalate levels to which 25% of American women are exposed

Altered genital development in baby boys
OR= 47 95% CI 5.5 - >1000

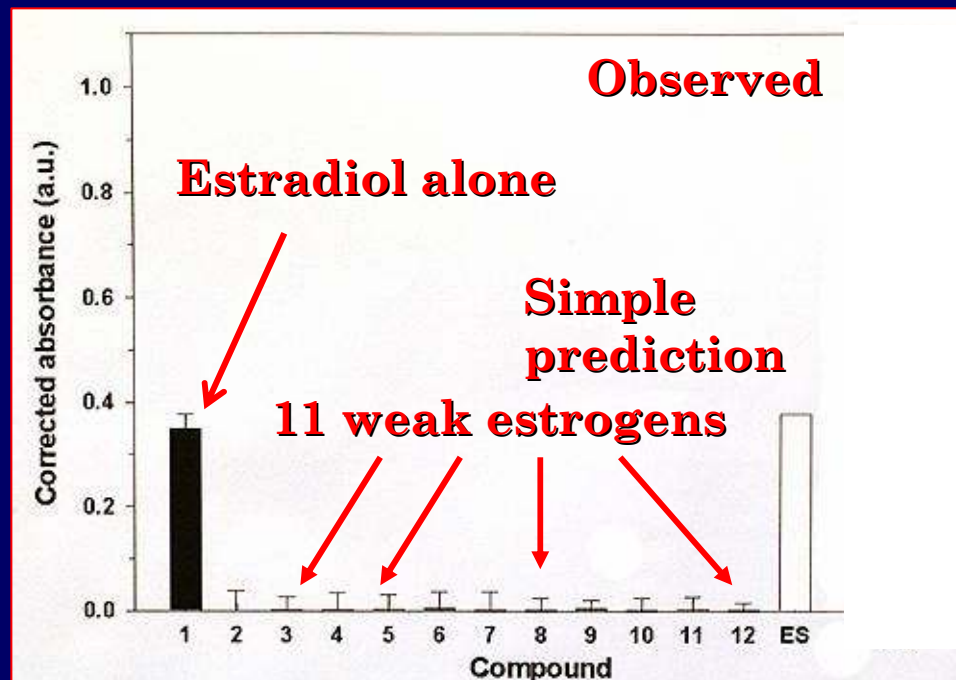
Swan *et al.* 2005



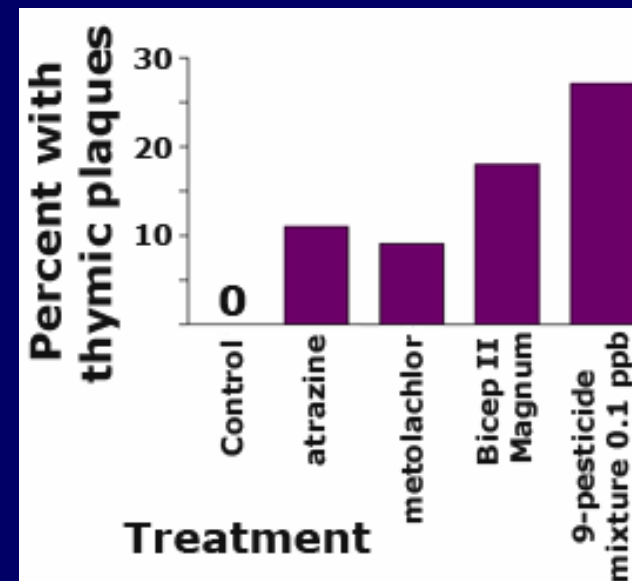
Mixtures interact

CDC NHANES data, among many:

Hundreds of chemicals present



Mixtures: Unexpected results



Hayes *et al.* 2006



- Some contaminants can alter gene behavior at **extremely low doses**.
- Adult diseases and sensitivity to subsequent exposures can be **programmed during development**.
- High dose experiments don't predict those **low dose impacts**.
- Mixtures are ubiquitous; they alter impacts, sometimes **unpredictably**



Bad news...

Today's health standards have been blind-sided by these scientific discoveries. **They are too weak.**

Good news...

Diseases caused by contaminant-altered expression of genes can be prevented... **if we modernize health standards.**



Plausible links to bisphenol A based on animal experiments

Impaired brain development

Hyperactivity

Long-term memory formation

Aneuploidy: Down's syndrome

Dementia

Prostate cancer

Breast cancer

Low sperm count

Obesity and diabetes

