Epidemiology of PFAS

Community Advisory Board Meeting

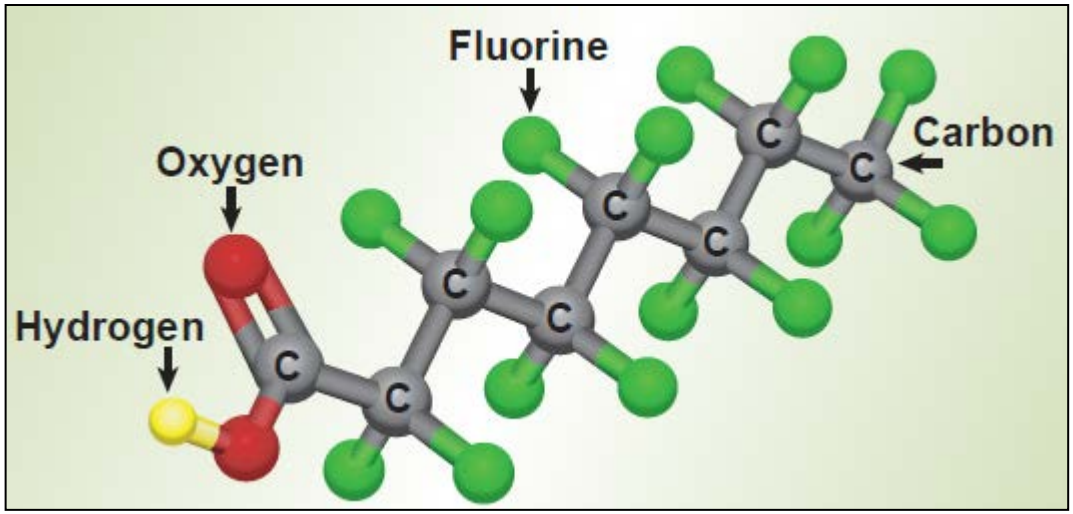
June 2, 2015

Courtney Carignan, Ph.D.

Summary

1. Background
2. Health effects review
3. Health studies

Perfluorinated alkyl substances (PFAS, aka PFCs)



Hydrophilic functional group
Hydrophobic/lipophilic fluorinated tail
C-F bond is very strong – does not break down easily

Perfluorinated alkyl substances (PFAS, aka PFCs)

Widely used in the manufacture of products resistant to stains, grease and water.

- Sofas and carpets stain resistant
- Food packaging (microwave popcorn, pizza boxes, parchment paper)
- Water/stain-proof clothing and mattresses
- Production of non-stick cookware
- Some firefighting foams

A Group of Chemicals

Name	Acronym
Perfluorobutane sulfonate	PFBS
Perfluorohexane sulfonate	PFHxS
Perfluorohexanoic acid	PFHxA
Perfluorooctanoic acid	PFOA
Perfluorooctane sulfonate	PFOS
Perfluorononanoic acid	PFNA
Perfluorodecanoic acid	PFDA
8+2 Fluorotelomer alcohol	8:2 FTOH

C8

Pease

Half-life

Time it takes for half of the chemical present to be removed from the blood

~3 years	Perfluorooctanoic acid	PFOA	C8
~5 years	Perfluorooctane sulfonate	PFOS	Pease

Properties of Concern

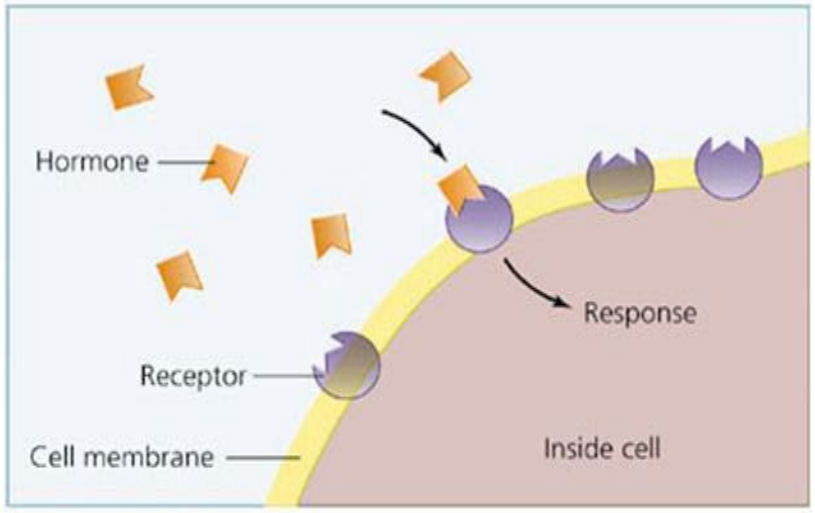
- Widespread presence in general population
- Long half-lives
- Transfer from mother to fetus
- Presence in breast milk

Health Effects Review

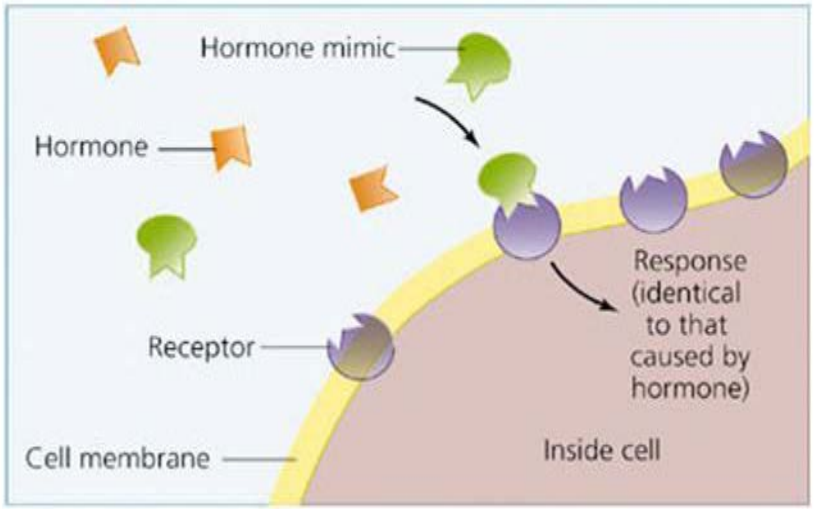
1. Endocrine disruption
2. Developmental origins of disease
3. Review some epidemiologic studies

Endocrine Disrupting Chemicals

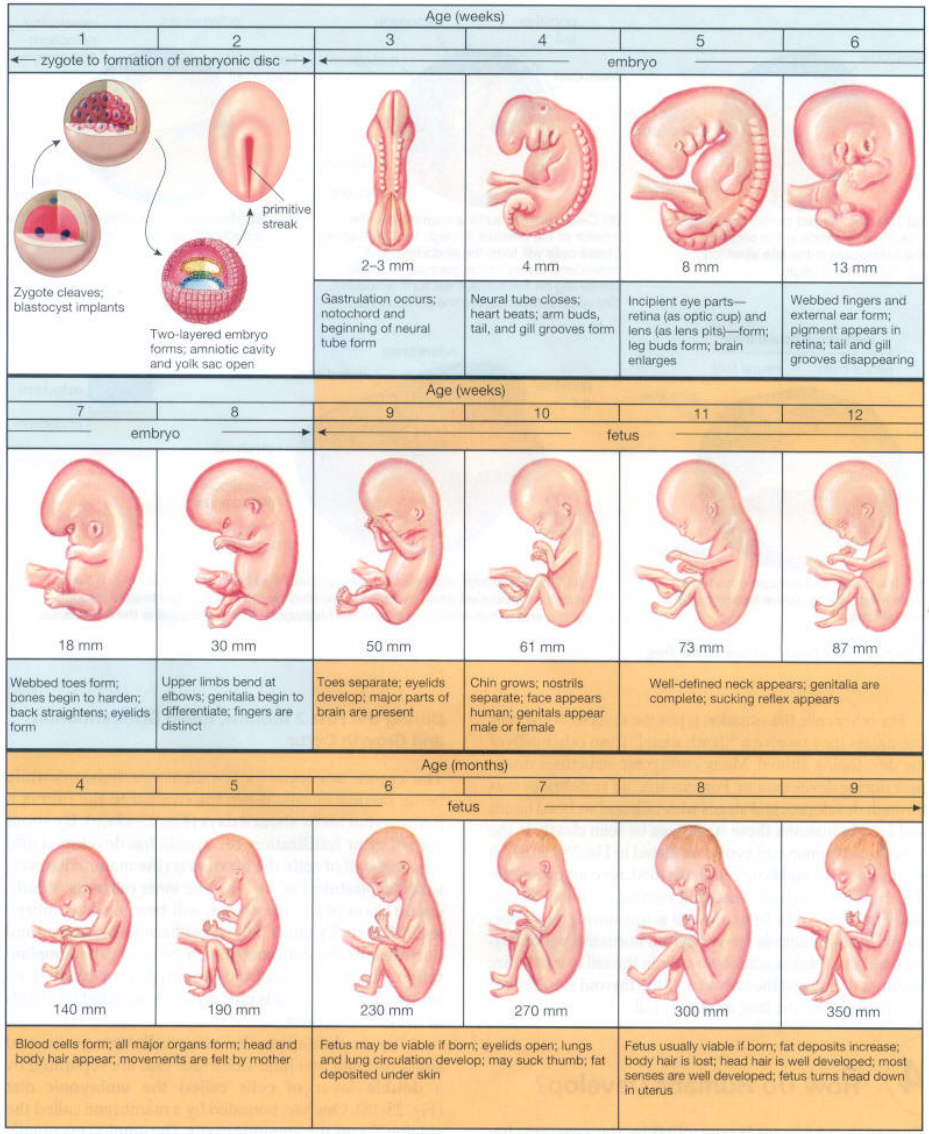
Chemicals that interfere in some way with the body's hormone system.



(a) Normal hormone binding



(b) Hormone mimicry



Development and Early Life is Sensitive to Endocrine Disruption

Fetus, Infants and Children

1. Sensitive to endocrine disrupting chemicals
2. Developing enzymes to metabolize chemicals
3. Higher exposure by body weight

Mother:Child Ratio of PFOS

- PFOS was an average of 42% higher in children compared to mothers
- Persisted until at least 19 years of age
- Boys older than 5 had significantly higher PFOS child:mother ratios than girls

C8 Health Study:
(Mondal et al. 2012)

Thyroid Hormone

C8 Health Study:

- Prenatal PFOS associated with an increase in T_4 among children 1-17 years old (Lopez-Espinosa et al. 2012)

Pregnant Norwegian women:

- PFOS positively associated with thyroid stimulating hormone (TSH) (Wang et al. 2013)

General Health Outcomes of concern for EDCs

- Fertility and Fecundity
- Neurodevelopment
- Immune function
- Timing of puberty
- Metabolic syndrome
- Hormonally sensitive cancers

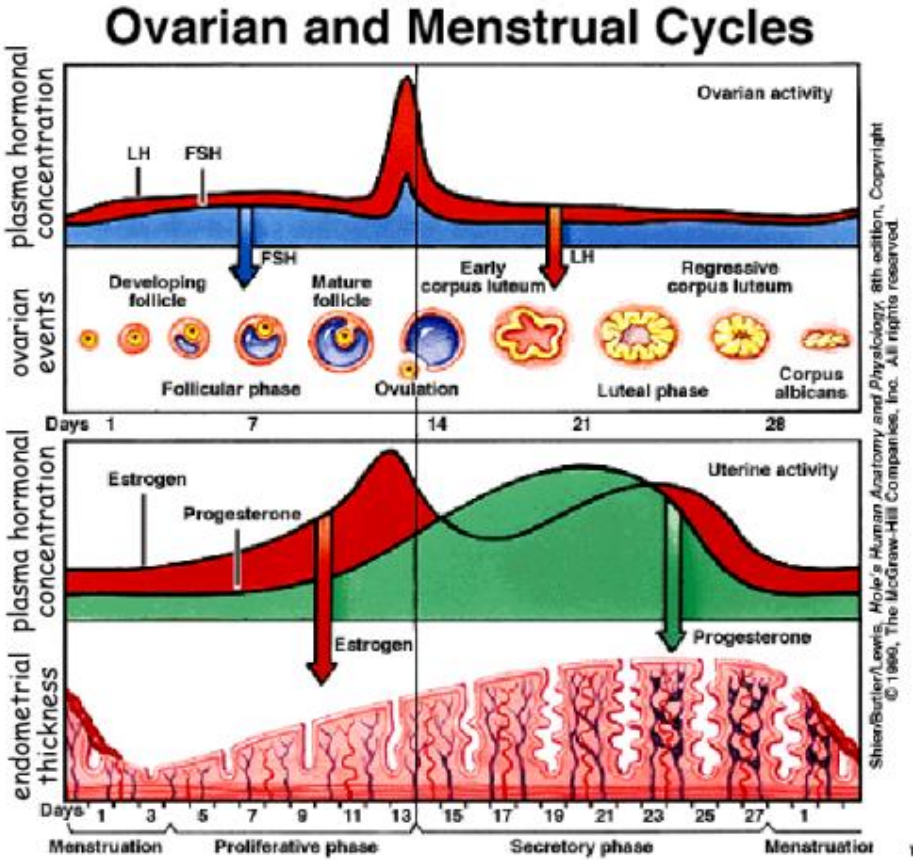
Examples of specific epidemiologic studies

- For contextual purposes, not a comprehensive literature review

Female reproduction

PFOS associated with lower concentrations of ovarian hormones, E_2 (estrogen) and progesterone

(Knox et al. 2011, Barrett et al. 2015)



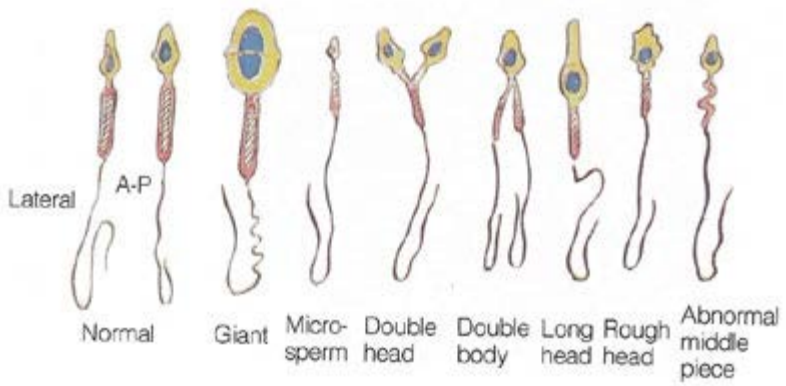
Female reproduction

PFOA and PFHxS (but not PFOS) associated with increased fecundability (time to pregnancy) and increased odds of infertility (Valez et al. 2015)

Male reproduction

Developmental exposure:

- PFOA: Lower sperm concentration and sperm count (Vested et al. 2013)
- PFOS: 35% reduction in morphologically normal sperm (Toft et al. 2012)



Neurodevelopment

General Danish Population:

- No association between prenatal PFAS exposure and risk of ADHD or childhood autism (Liew et al. 2015)

C8 Health Study:

- Increase in prevalence of ADHD with increasing prenatal PFHxS exposure (Stein and Savitz 2011)

Immune Function - Children

- Doubled concentrations of PFOS at age 5 were associated with increased odds of falling below a clinically protective level of tetanus and diphtheria antibodies at 7 years of age (Grandjean et al. 2012)

- Maternal serum PFOA associated with decreased vaccine responses and increased frequencies of common cold and gastroenteritis (Granum et al. 2013)

Immune Function - Adults

C8 Health Study

Elevated PFOA associated with:

- Reduced antibody titer rise (especially influenza)
- Increased risk of not attaining antibody threshold for long-term protection

(Looker et al. 2013)

Timing of Puberty

C8 Health Study:

- PFOS exposure associated with longer time to puberty among both boys and girls (~100 days, on average) (Lopez-Espinosa et al. 2012)

Danish cohort:

- Daughters exposed to higher levels of PFOA in utero reached puberty 5.3 months later (Kristensen et al. 2013)

Cholesterol

C8 Health Study:

- In children, increased risk for abnormal total-C and LDL-C with increasing PFOS and PFOA (Frisbee et al. 2011)
- In adults, increase in total-C and LDL-C with increasing PFOS and PFOA (Steenland et al. 2009)
- In women, PFOS was associated with expression of genes involved in cholesterol mobilization and transport (Fletcher et al. 2013)

Hormonally Sensitive Cancers

C8 Health Study (only PFOA was assessed):

- Testicular cancer: 3 fold increase in odds
- Ovarian and prostate cancer: Increased odds (not statistically significant but low statistical power)

(Barry et al. 2013)

Workers: Excess testicular and prostate cancers

Animals: Increased male reproductive organ cancer, delay in mammary gland development

Other Cancers

C8 Health Study (only PFOA was assessed):

- Kidney cancer: 2 fold increase among women (but not men)
- Non-Hodgkin lymphoma: 80% increase among most highly exposed

(Barry et al. 2013)

Workers: Excess kidney and bladder cancer as well as myeloid leukemia

Review of concerns

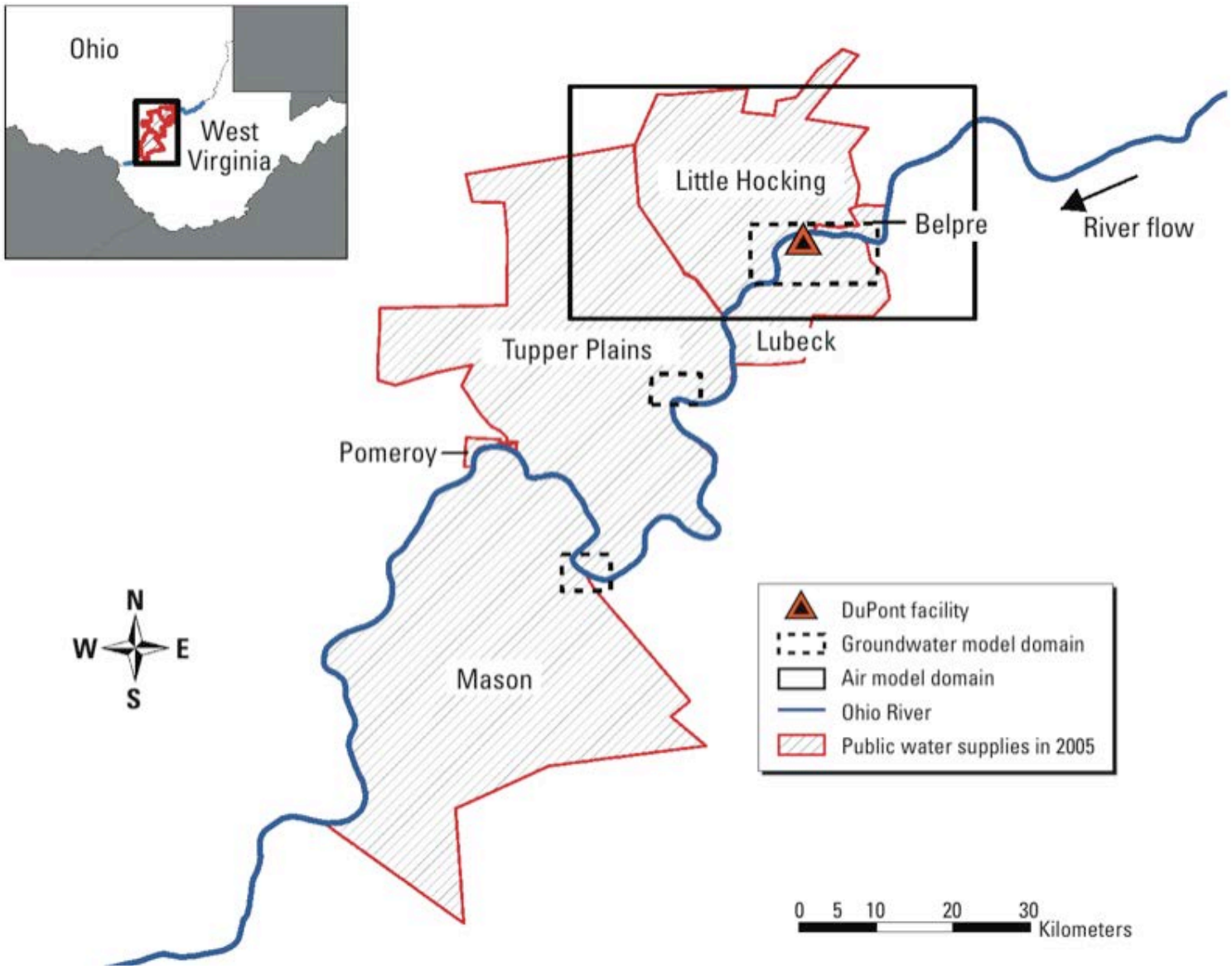
- Fertility and Fecundity
- Neurodevelopment – ADHD*
- Immune function – children* and adults
- Delayed puberty *
- Cholesterol - children* and adults
- Cancer – testicular and kidney

* Prenatal exposure

Health Studies

1. Ongoing health studies
   - C8
   - Ronneby
2. Types of health studies

C8 Health Project



C8 Health Project

- 69,030 residents enrolled from 2005-2006
- Demographic data, medical diagnoses, clinical laboratory testing, serum PFCs
- High exposures to PFOA, PFOS levels lower
  - Although drinking water ranged up to 4,900 ng/L

- C8 Science Panel Website: http://www.c8sciencepanel.org/publications.html

Ronneby, Sweden

- Elevated PFOS in drinking water discovered in 2013, 4,000 ng/L
- Air force base
- Fire-fighting foam
- 5,000 households affected

Jakobsson 2015

Drinking water (ng/L)

	Pease	Ronneby
Perfluorooctane sulfonate (PFOS)	2500	4000
Perfluorohexane sulfonate (PFHxS)	830	1200
Perfluorooctanoic acid (PFOA)	350	130
Perfluorohexanoic acid (PFHxA)	330	340
Perfluoropentanoic acid (PFPeA)	270	52
Perfluoroheptanoic acid (PFHpS)	120	67
Perfluorobutane sulfonate (PFBS)	51	140
Perfluorononanoic acid (PFNA)	17	1.2
Perfluorodecanoic acid (PFDA)	4.9	< 1
Perfluoroundecanoic acid (PFUnA)	< 1	< 10
Perfluorododecanoic acid (PFDoA)	< 2	< 10
	4451	5789

Ronneby, Sweden Preliminary Risk Assessment

- TDI exceeded in formula-fed infants
- No acute health effects
- Probably no increased risk for adverse health effects on individual health in the long run
- Possibly detectable effects on the population level

Jakobsson 2015

Ronneby, Sweden Pilot Study

- Compared blood levels in school children with (n=20) and without (n=20) PFOS in drinking water
- Levels in exposed children highly elevated

Ronneby, Sweden Exposure Monitoring

- Collected blood from 2,600 affected residents (of ~9,000 total)
- Focus on those under and approaching reproductive age
- In blood: Measuring PFCs, lipids, thyroid hormone, metabolomics, epigenetic markers

Jakobsson 2015

Ronneby, Sweden Pregnancy Cohort

- ~300 births/year
- Maternal blood from pregnancy, at birth, at 6-8 weeks postpartum and after lactation
- Placenta, colostrum, mature breast milk
- Child immunity

Jakobsson 2015

Community Health Guide

1. What is a health study and why would you want one?
2. Framing your concern as a research question
3. A Menu of Health Studies

http://www.bu.edu/sph/files/2015/03/HSG_5-14-2015_nocover.pdf

Positive things a health study might do:	Negative things a health study might do:
• Document disease and/or exposure • Demonstrate a relationship between exposure and disease • Educate residents about environmental health concerns • Generate media coverage and motivate the community • Be useful for political leverage in a campaign • Create an opportunity for members of your community to get involved • Be useful in community efforts to protect the health of future generations	• Document no significant relationship between a disease and exposure • Appear to show that there is no problem • Give permission to polluters to continue polluting • Lead to legal issues over confidentiality or lawsuits by polluters • Be used against your campaign or group • Overwhelm your organizing efforts and sap members' energy • Generate statistics that may undermine your efforts • Identify health problems that you are unprepared to deal with • Delay action while waiting for results

Types of Studies

Studies of Exposure

- Environmental or personal exposure monitoring
- Body burden / biomonitoring
- Environmental impact statements

Studies of Outcome

- Community survey
- Analysis of registry data

Studies of the Exposure-Outcome Relationship

- Ecologic study

Ronneby → Cohort study

Cancer → Case-control study

Studies of Contaminated Sites

- Risk assessment
- Public health assessment

Suggestions moving forward

1. Use existing studies, biomonitoring data and community concerns to identify health concerns
2. Frame questions
3. Consider options for addressing those questions

THANK YOU

carignan@hsph.harvard.edu

Exposure Misclassification

How much water did you drink per week?

Drinking water at Pease (ng/L)

	Harrison	Smith	Haven
Perfluoropentanoic acid (PFPeA)	7.9	3.5J	270
Perfluorobutane sulfonate (PFBS)	2J	0.94J	51
Perfluorohexanoic acid (PFHxA)	8.7	3.9J	330
Perfluoroheptanoic acid (PFHpS)	4.6J	2.5J	120
Perfluorohexane sulfonate (PFHxS)	36	13	830
Perfluorooctanoic acid (PFOA)	9	3.5J	350
Perfluorononanoic acid (PFNA)	NDU	NDU	17
Perfluorooctane sulfonate (PFOS)	48	18	2500
Perfluorodecanoic acid (PFDA)	NDU	4.4J	4.9J
Perfluoroundecanoic acid (PFUnA)	NDU	17	NDU
Perfluorododecanoic acid (PFDoA)	NDU	12	NDU
	116.2	49.7	4473

Developmental Origins of Disease

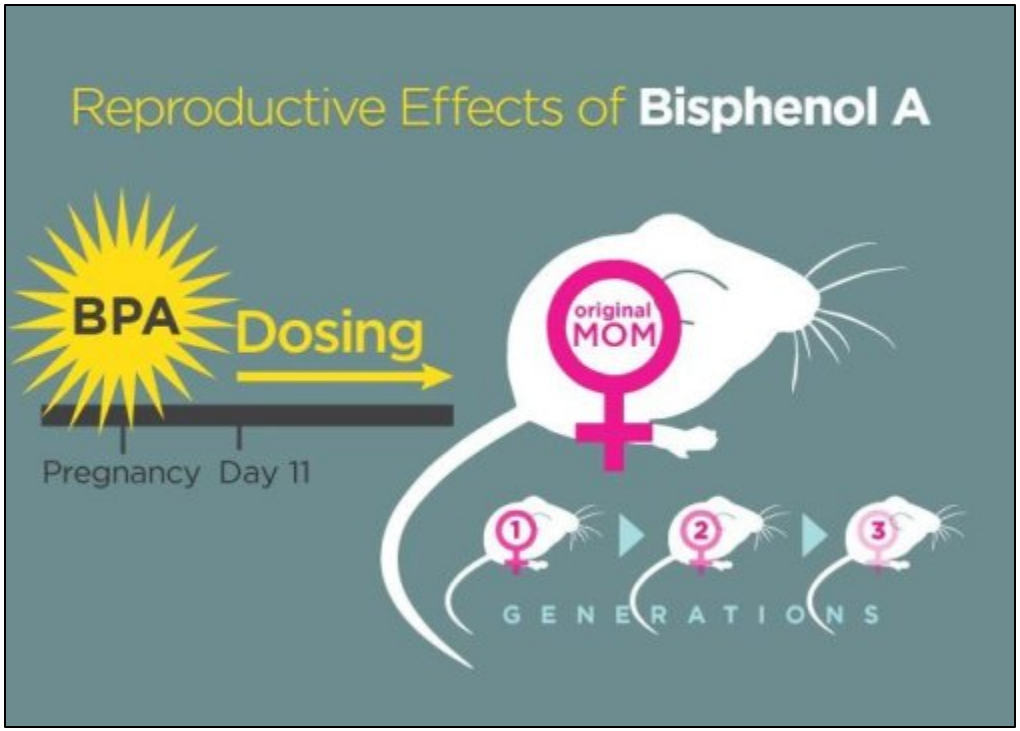


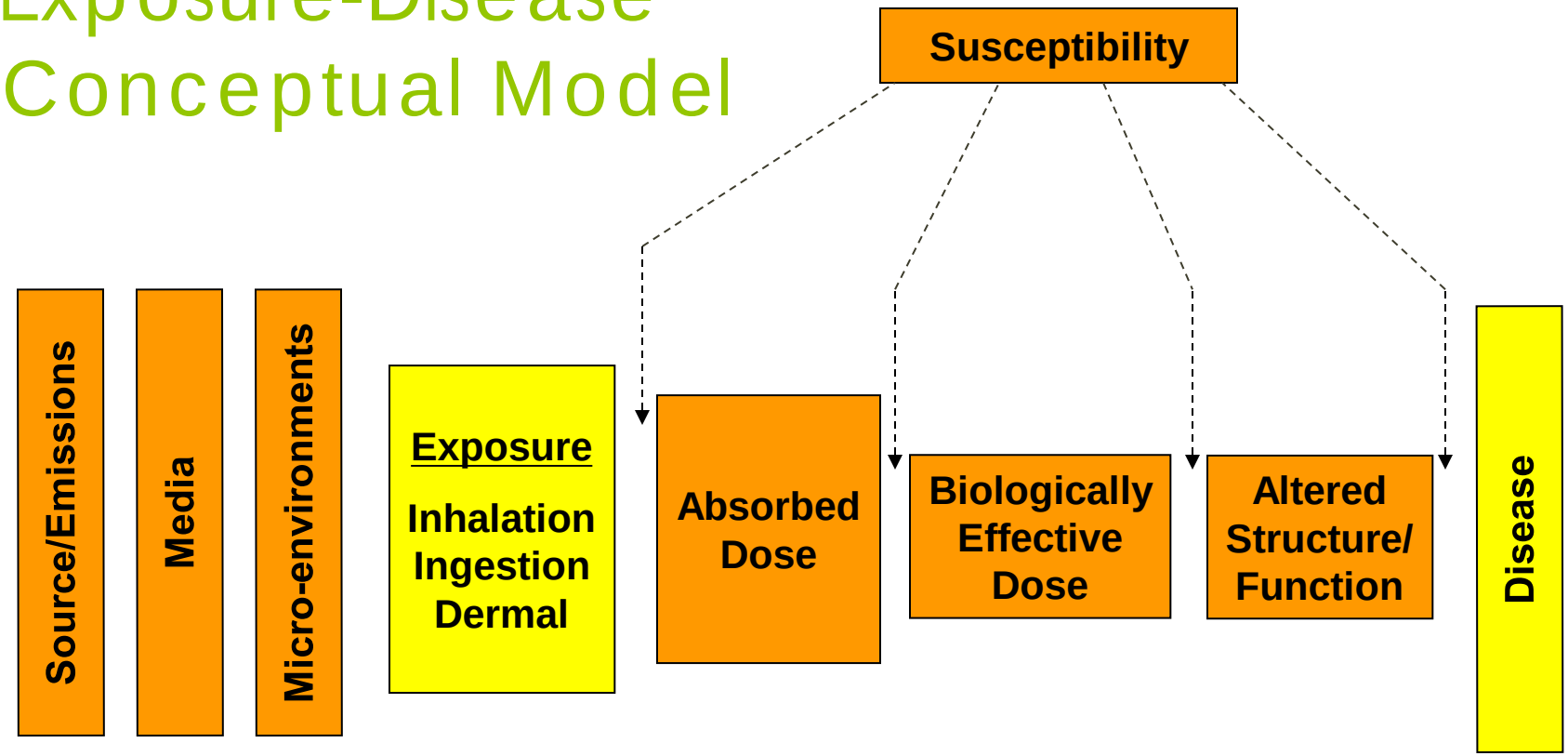
Table 6-2. Comparison of PFOA content ranges between this study and literature values (in ng PFOA/g sample, unless indicated otherwise)

Article category	Literature [a]	This study [a]
Pre-treated carpeting	200 to 600 [b]	ND (<1.5) to 462
Carpet-care liquid treated carpeting	200 to 2000 [b]	0.6 to 224 [c]
Treated apparel	ND (<20) to1400 [b]	5.4 to161
Treated upholstery	ND (<34) [b]	0.6 to 293
Treated home textiles	ND (<20) to 1400 [b]	3.8 to 438
Treated non-woven medical garments	ND (<34) [b]	46 to 369
Industrial floor wax and wax removers	0.5 to 60 [b]	7.5 to 44.8
Stone, tile, and wood sealants	ND (<100) [b]	477 to 3720
Membranes for apparel	0.008 to 0.07 ng/cm^2 [b]	0.1 to 2.5 ng/cm^2
Food contact paper	6 to 290 [d]	ND (<1.5) to 4640
Dental floss/tape	3 to 4 [d]	ND (<1.5) to 96.7
Thread sealant tape	1800 [d]	ND (<1.5) to 3490
PTFE cookware	4 to 75 [d]	ND (<1.5) to 4.3

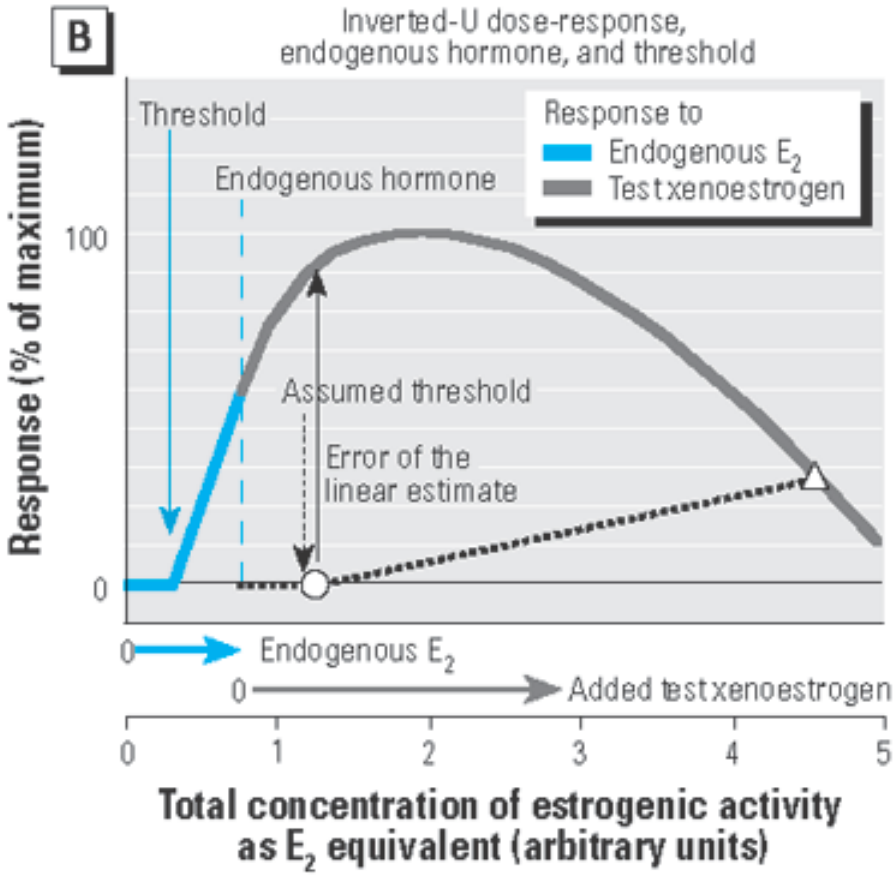
[a] ND: not detected (detection limit in parentheses). [b] Data source: ref 7 (based on theoretical calculations). [c] Calculated by using the recommended coverage and assuming the area density of the carpet is 0.25 g/cm^2. [d] Data source: ref 17.

U.S. EPA 2009

Exposure-Disease Conceptual Model

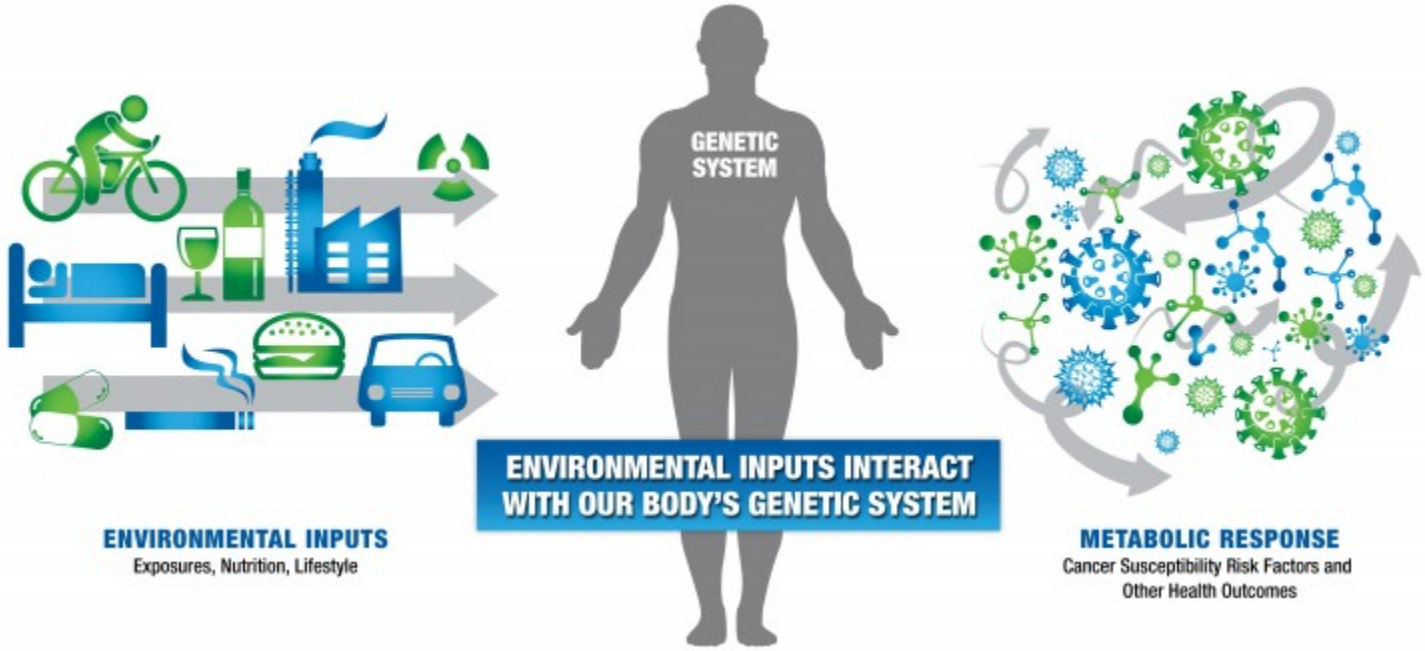


Non-Monotonic Dose Response



Welshons et al. 2003

Gene-Environment



Gene-Environment