PHTHALATES:

LATEST RESEARCH FROM THE UNIVERSITY OF ROCHESTER

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December 12, 2013

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Disclosures

No conflicts or financial interests.

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Outline

- ***Background***
  - What are phthalates and where are they found?
  - Why are we concerned about them?
  - The “phthalate syndrome”

- ***Recent research at University of Rochester***
  - The Infant Development and the Environment Study (TIDES)
  - Dietary intervention pilot study
  - Future directions

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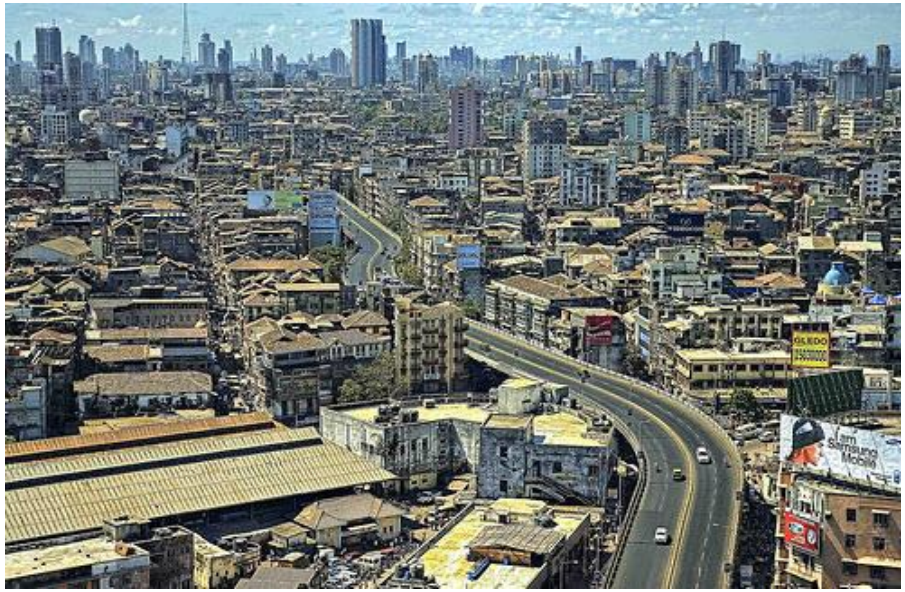
Industrialization



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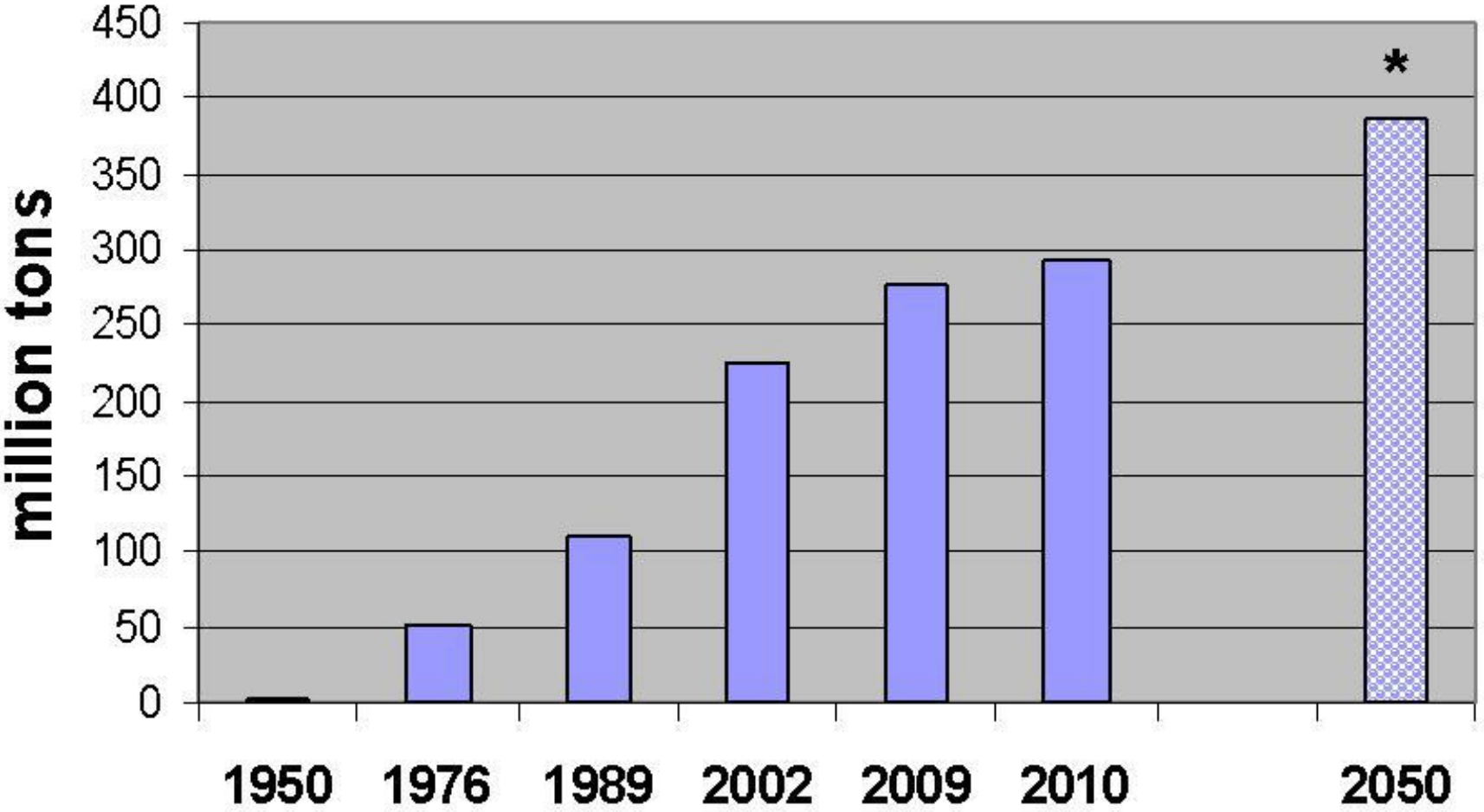
Annual World Plastics Production



Source: PlasticsEurope Market Research Group

Where are phthalates found?

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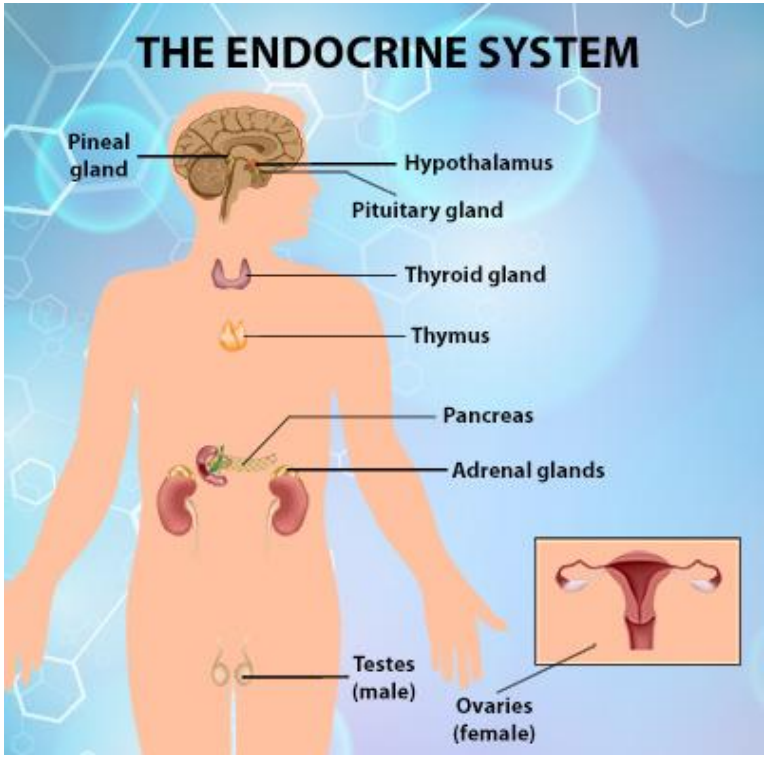
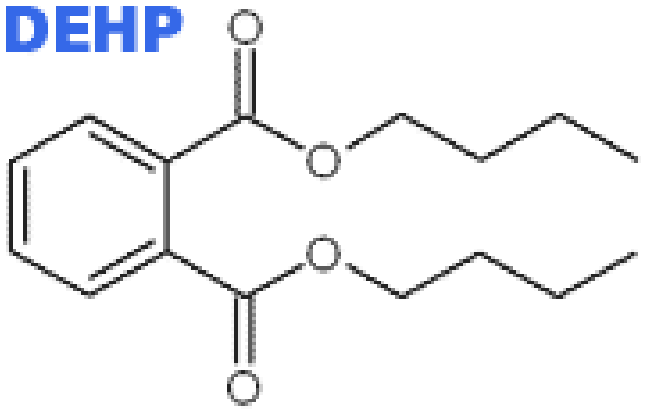
Why do we care that we are all exposed to these chemicals?

Endocrine-Disrupting Compounds (EDC)





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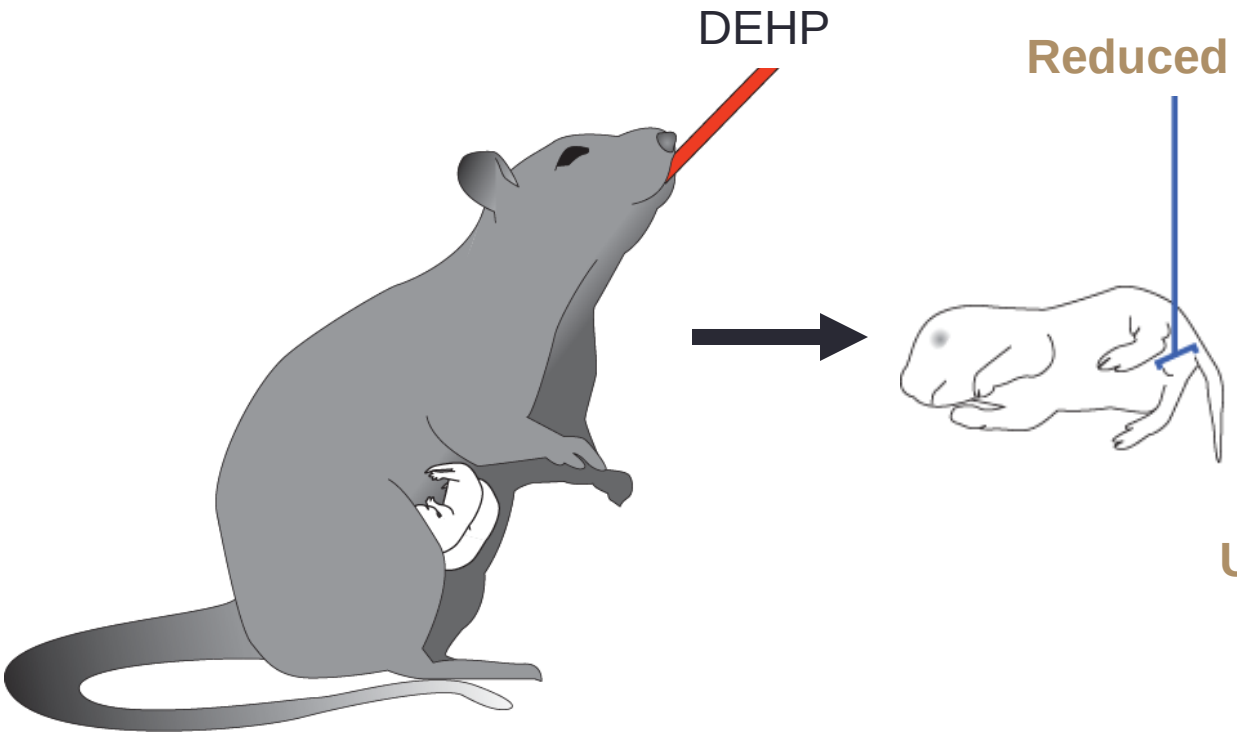
The Phthalate Syndrome



Reduced AGD

Malformations of
Epididymis
Vas deferens
Seminal Vesicles
Prostate

Hypospadias
Undescended Testicles

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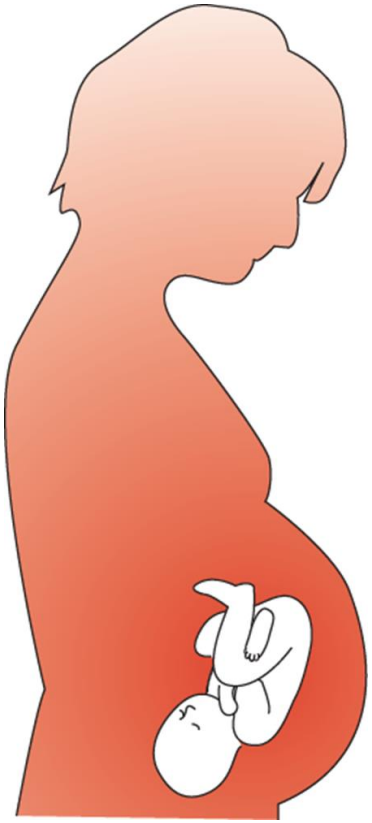
Gray and Foster 2003, Foster 2005

What about in humans?



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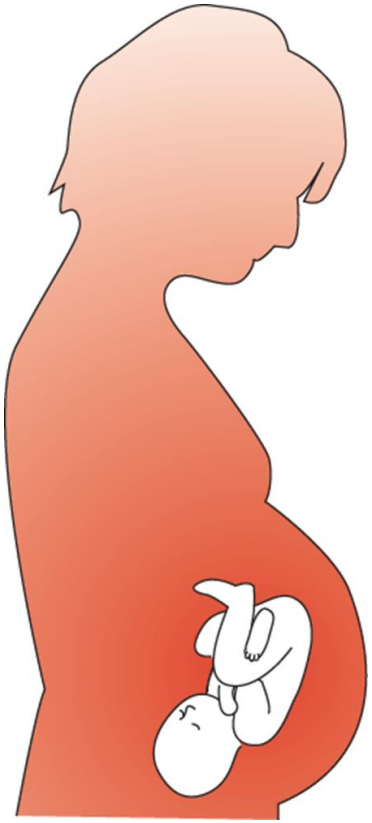

Can phthalates alter AGD in humans?

Can they cause the “phthalate syndrome”?

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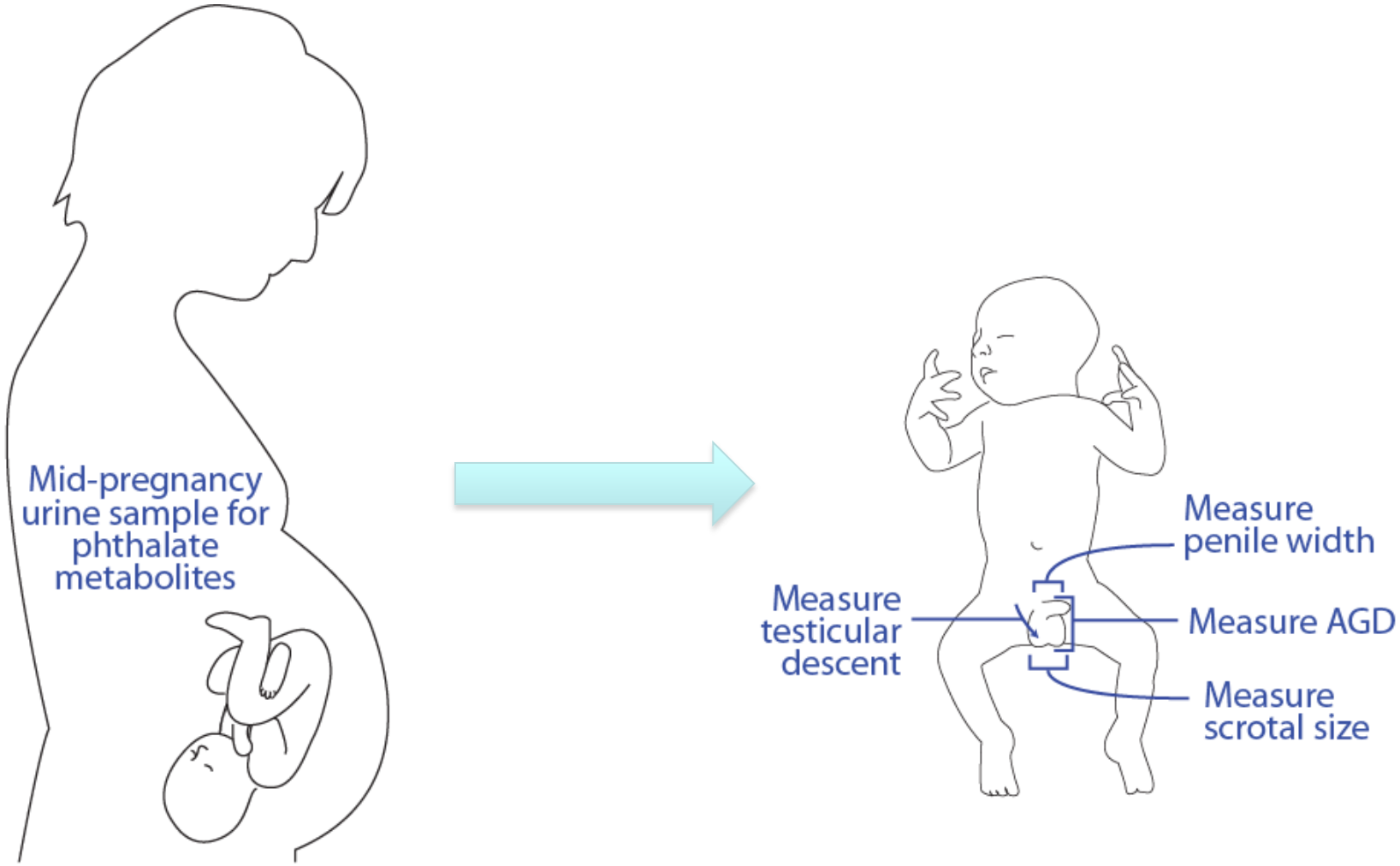
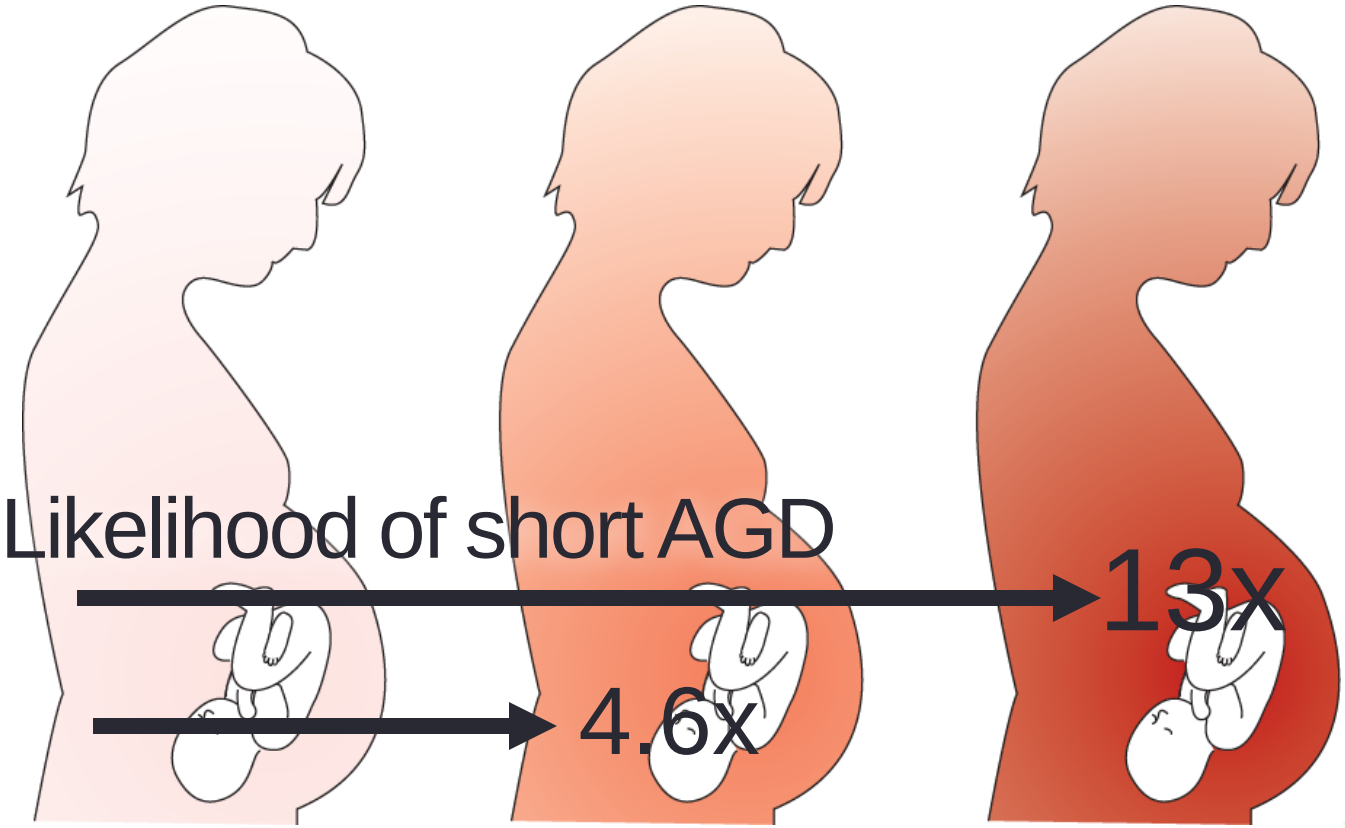
Human studies…



	Percentile (ng/mL)		
Monoester Metabolite	**25th**	**50th**	**75th**
MEHHP	6.0	11.4	20.1



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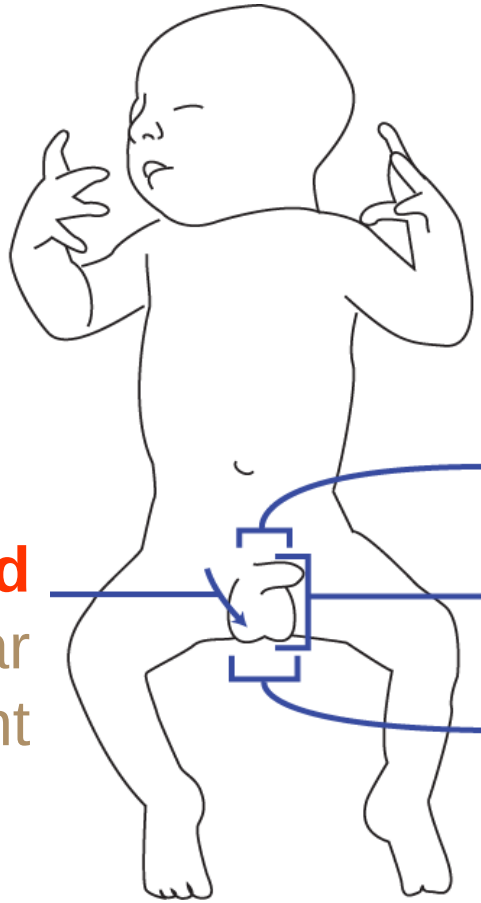
Higher phthalate exposure was also associated with other genital endpoints



Reduced penile width

Decreased testicular descent

Reduced AGD

Reduced scrotal size

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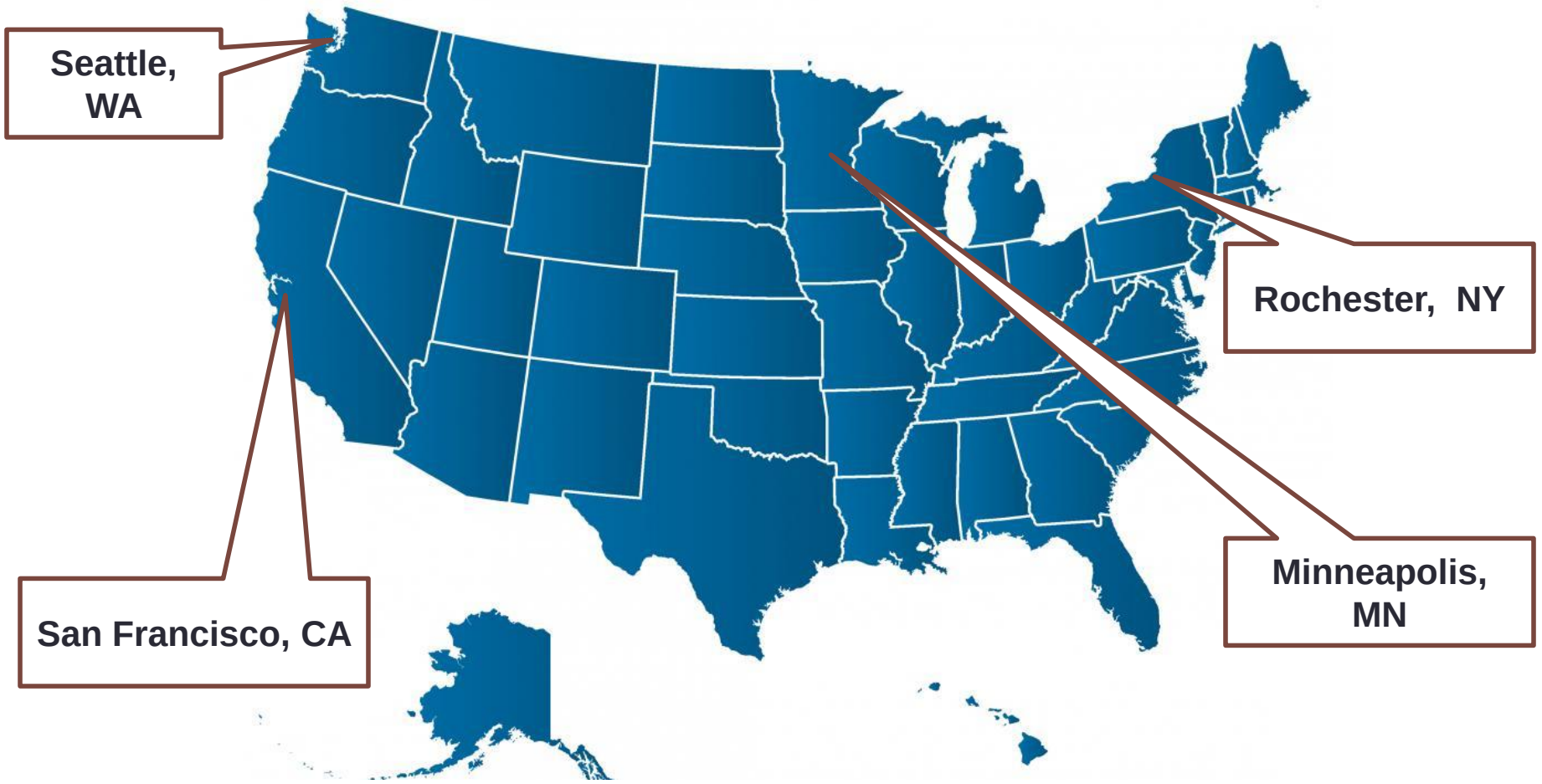
Swan et al 2005, 2008

TIDES Population

1st trimester pregnant women from four study centers (n=875)



The Infant Development and the Environment Study (TIDES)

- **PHASE I**:
  - Urine in each trimester
  - Blood at 12-14 weeks
  - Questionnaires in each trimester
- **PHASE II**: Birth exam of male and female newborns including AGD measurements (n=718)
- **PHASE III**: 12-month follow-up exam of male infants (underway)

TIDES Study Aims

We are currently examining:

1) Prenatal phthalate exposure and anogenital distance (AGD)

We hypothesize that phthalate exposure is associated with shorter AGD in boys, but not girls.

2) Critical periods of exposure

We hypothesize that the first trimester is the critical period during which phthalates can affect reproductive development.

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Is phthalate exposure dropping?

Median phthalate metabolite concentrations (ng/mL)

	NHANES 2003-2004	SFF * 2000-2003	NHANES 2009-2010	TIDES* 2010-2012
MEHP	3.0	3.3	1.3	2.6
MEHHP	10.9	11.4	11.6	7.5
MEOHP	9.5	11.1	7.4	5.5
MBzP	10.8	8.3	6.4	3.9
MiBP	2.8	2.5	7.5	5.0
MEP	129	128	60	30.2

* Pregnant women

And if so, why?

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Geographical differences: How does Rochester compare?

Mean USG-adjusted phthalate metabolite concentrations by study center (ng/mL)				
	San Francisco	Minneapolis	Rochester	Seattle
	N=156	N=185	N=191	N=137
mHINCH	0.88	0.45	0.4	0.43
MBP	11.92	11.04	17.95	9.52
MBzP	5	7.76	12.34	6.42
MCNP	3.41	4.26	5.14	4.75
MCOP	17.89	51.14	75.24	39.12
MECPP	2.84	8.58	15.49	4.21
MECPP	11.27	14.51	19.64	25.17
MEHHP	10.86	11.5	17.78	25.83
MEHP	3.37	3.89	6.09	6.91
MEOHP	7.25	7.86	11.89	17.19
MEP	79.49	119.19	210.88	84.07
MIBP	6.03	7.16	10	5.45
Sum DEHP	11.04	12.71	18.67	25.31

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The bigger picture

Why are these subtle changes in reproductive development important?

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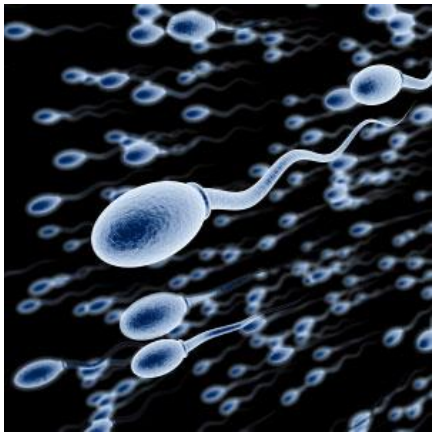
Why are these subtle changes in reproductive development important?

- AGD may be an indicator of reproductive health
- Rochester Young Men's Study (RYMS):

  short AGD → low semen quality!



- 20% met the criteria for low sperm count (<20 million/mL) even higher in African-American men) (Mendiola et al. 2011)

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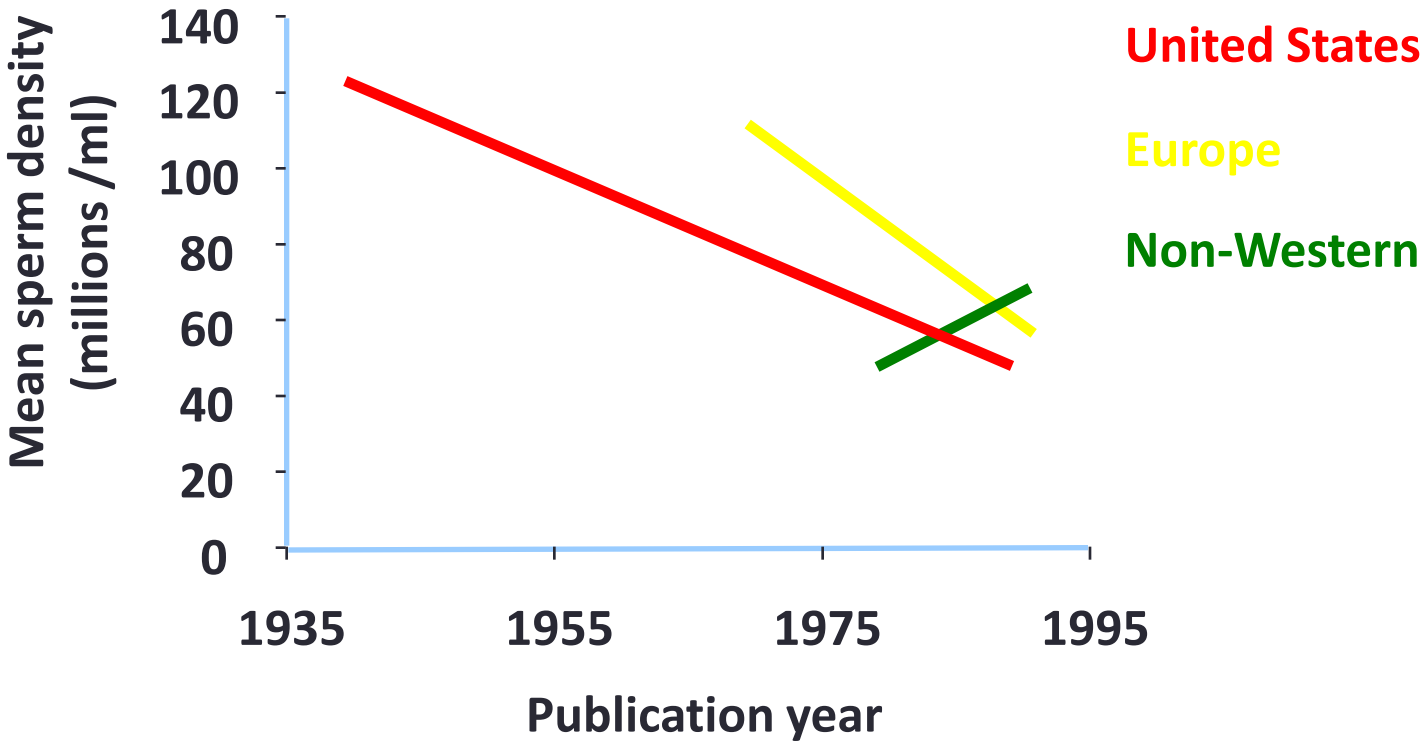
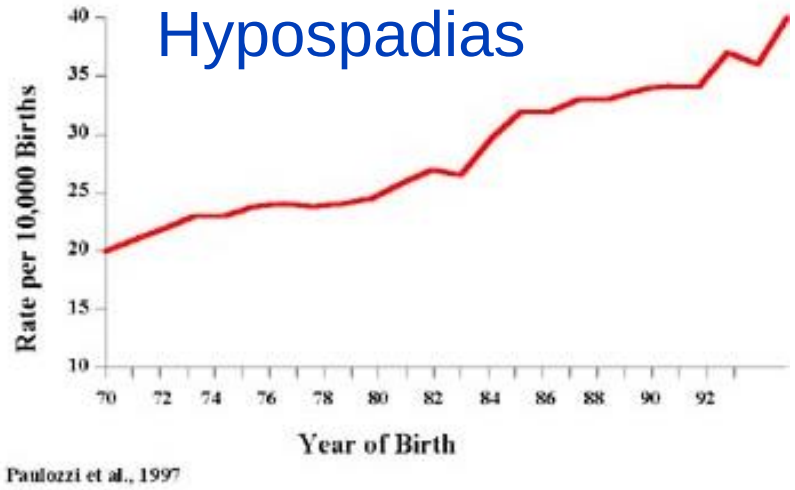
Trends in Sperm Count



Swan et al. 2000 (reanalysis of Carlsen et al 1992)

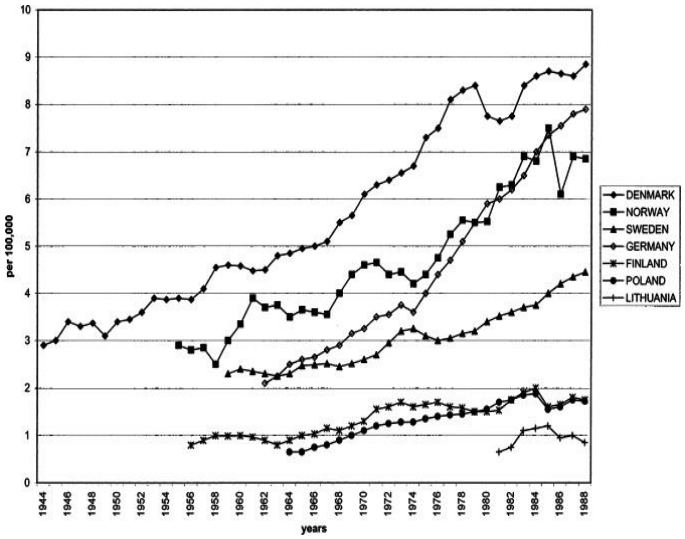
Male Reproductive Development: Global Trends

Hypospadias



Paulozzi et al., 1997

Testicular cancer



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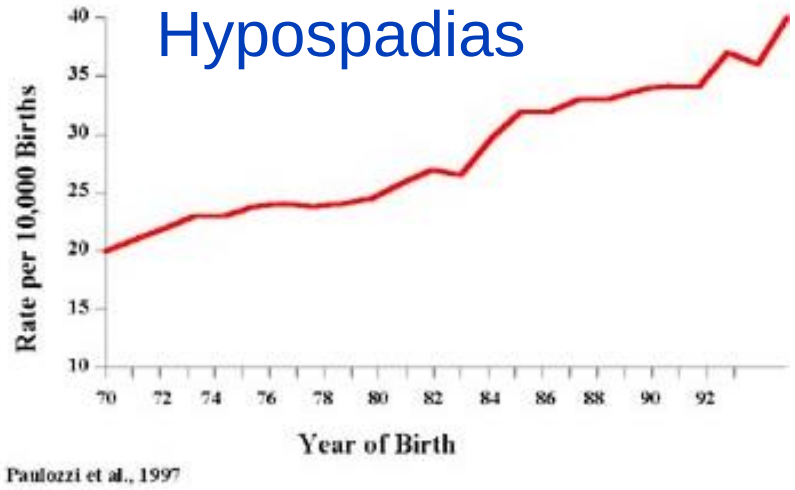

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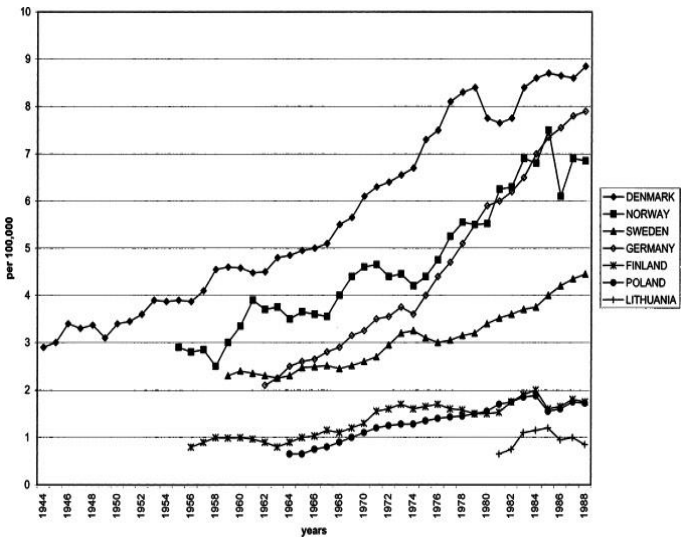

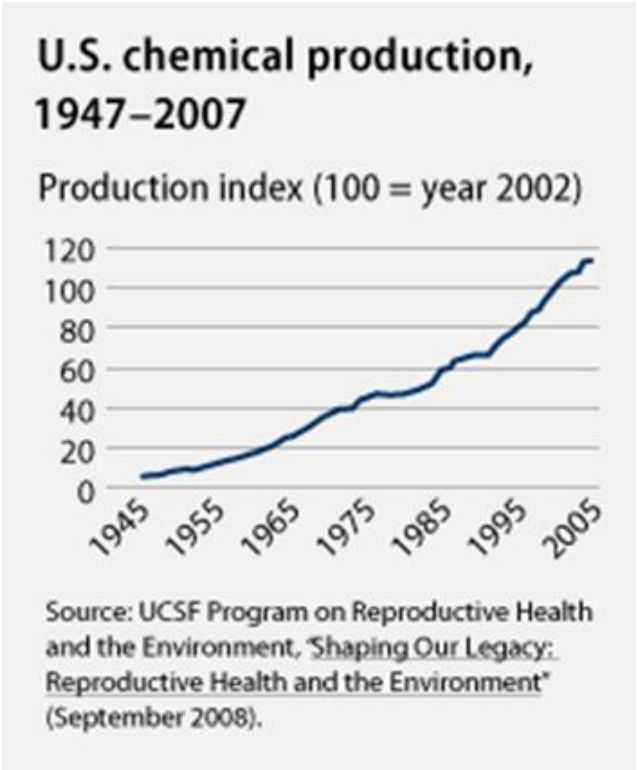

How can we reduce our exposure to phthalates?

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How can we reduce our exposure to phthalates?

- Diet is the greatest source of DEHP
- Main dietary sources are somewhat unclear, but highest DEHP concentrations

  seem to be in fatty foods
  - Dairy
  - Cooking oils
  - Meat products

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Wormuth et al. 2006
Schecter et al. 2013
Bradley 2013
Cao 2010

As a rule…

The more manufacturing, processing, and packaging involved in food preparation, the more opportunity for phthalates to be introduced.

There may be migration from:

- Food processing films
- PVC tubing and gloves
- Inks used on packages
- Recycled paper used for packaging

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Can we lower our exposure to phthalates by changing our diet?

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“Temple Stay” Study

Day 1:
14:00 - Arrival & Registration (Uniforms distributed & rooms assigned)
15:00 – Opening Ceremony & Orientation
16:00 – Temple Tour and Rest
18:00 – Dinner
19:00 – Evening Buddhist Ceremonial Service
19:30 – Tea Ceremony & Conversation with Monks
20:30 – Preparing for Bed
21:00 – Bedtime

Day 2:
3:30 – Pre-dawn Buddhist Ceremonial Service
4:00 – Seon Meditation & Rest (Sitting and Walking Meditation)
6:00 – Breakfast
7:00 – Community Work
8:00 – Temple Tour
11:00 – Packing & Closing Ceremony
12:00 – Lunch
13:00 – Departure

Can we do this within industrialized society?

Can we do this within industrialized society?

Maybe…

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Can we do this within industrialized society?

Maybe…

but it's not as simple as you'd hope.

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A tale of two dietary interventions

Rudel et al (2011)

In 20 families who were high canned good consumers, 3 days on an organic, minimally processed diet lowered DEHP levels by over 50%

SUCCESS!

A tale of two dietary interventions

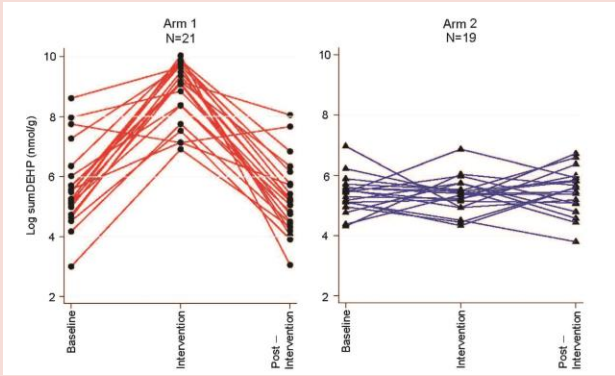
Rudel et al (2011)

In 20 families who were high canned good consumers, 3 days on an organic, minimally processed diet lowered DEHP levels by over 50%

SUCCESS!

Sathyanarayana et al (2013)

Recruited 10 families with high canned, processed food consumption. Fed half a minimally processed diet, gave the other half pamphlets on how to eat better.



FAILURE!

Dietary intervention in low-income, pregnant Rochester women

AIMS:

Can we lower phthalate exposure in this high risk group through a brief dietary intervention?

Can we work with women to develop doable guidelines for healthy eating during pregnancy?

Can women lower their phthalate exposure by following those guidelines on their own?

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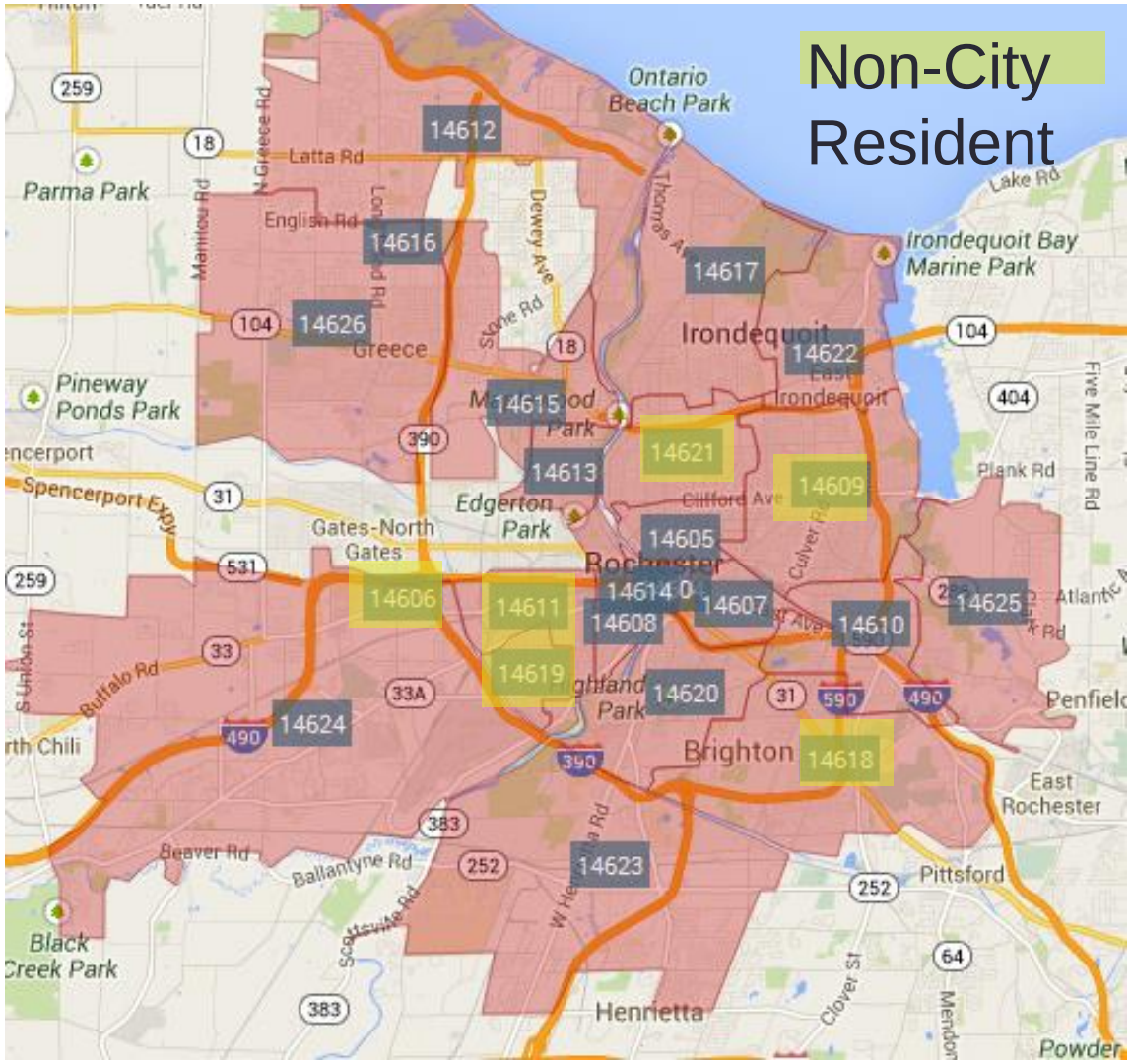
10 Participants



Income: Less than 25K per year

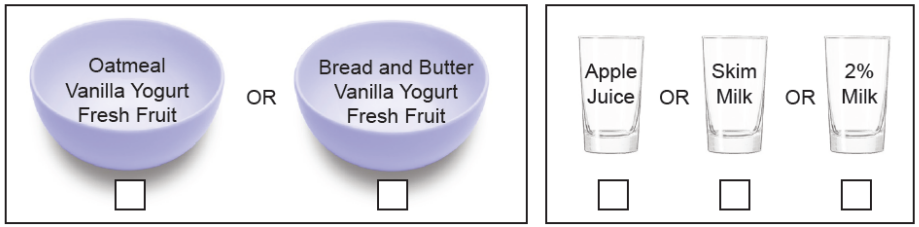
Average age: 26.4

6 African American
1 African American/Hispanic
2 Hispanic
1 Caucasian

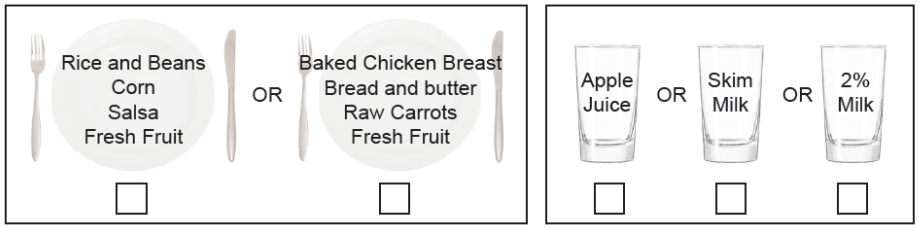
Not selected based on any typical dietary habits

The Food

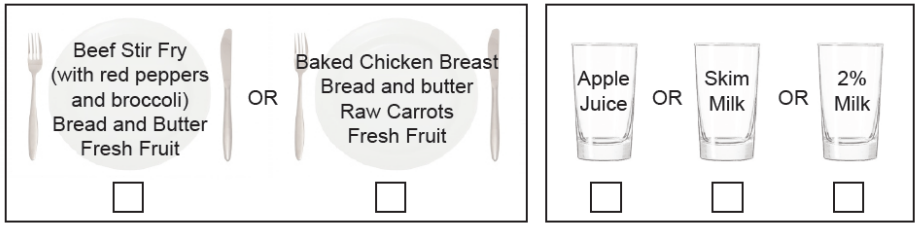
Breakfast



Lunch

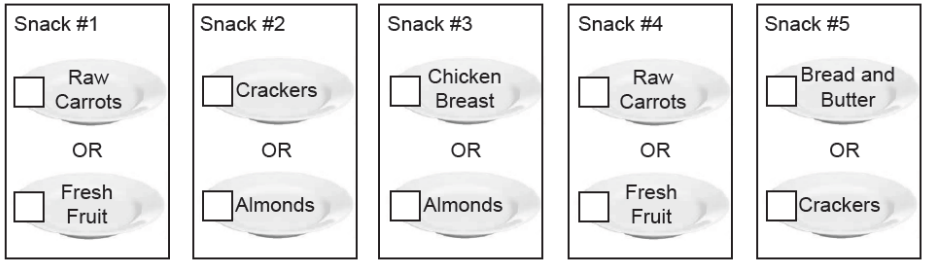


Dinner



Snacks

Only select if you are in your 2nd or 3rd trimester



Organic or BPA/Phthalate free products were used whenever possible.

No seasonings were added

Foods were stored in ziploc plastic containers and delivered to homes

Participants were asked to heat foods by microwaving on ceramic dishes or by stovetop on pans without non-stick coatings.

2 women were given glass plates because they did not have access to ceramic dishes.

What did the subjects think?

Their priorities:

- **Food needs to taste good**
- **Food needs to be easily and cheaply obtained**
- **Food needs to be easily prepared**

They wanted:

- **More variety**
- **More seasonings and condiments**
- **Snack foods**

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Our take-away messages:

- Among women with a “typical” diet (not high canned good and processed food eaters), attempts to lower phthalates through diet may not be effective
- Very difficult to know which foods/brands are highest in phthalates- “smartest” or “safest” choices are not obvious
- Women don’t want to sacrifice flavor/taste

If we want to reduce phthalate exposure through diet, it is not going to happen on an individual level- needs larger scale change!

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Future directions

- **TIDES II:**
  - Prenatal phthalate exposure and neurodevelopment
  - How do stress and phthalates interact to affect child development?
- **ECHO:** Environmental chemical, hormones, and the ovary
- **Hunter-gatherer study:** Are there any populations that are not exposed to these chemicals today?

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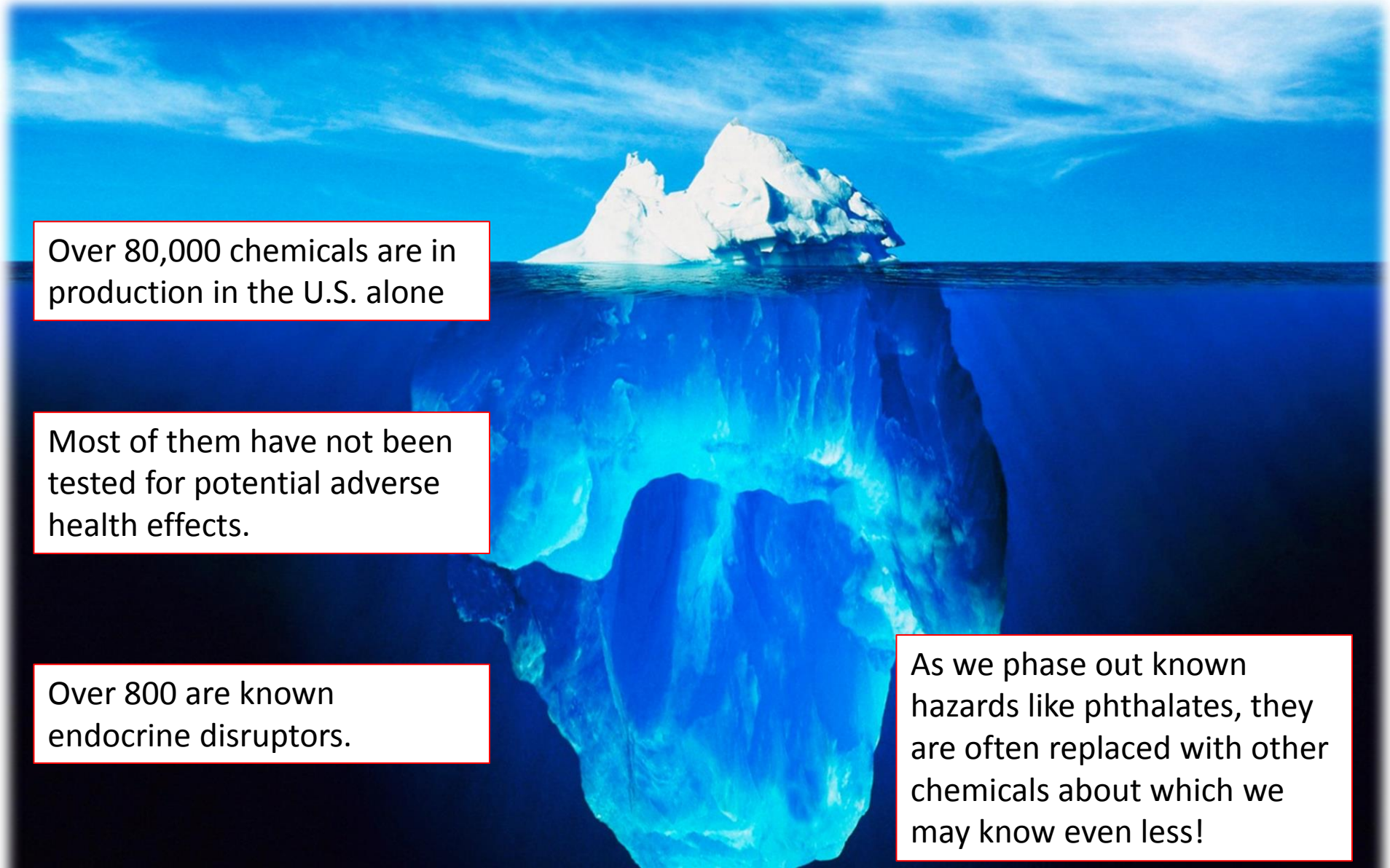
Phthalates are just the tip of the iceberg



Thanks to…

- **Collaborators:**
- Shanna Swan, PhD
- Shaw-Ree Chen, PhD
- Sheela Sathyanarayana, MD, MPH
  (University of Washington)
- J. Bruce Redmon, MD
  (University of Minnesota)
- Ruby Nguyen, PhD
  (University of Minnesota)
- Sarah Janssen, MD, PhD
  (UCSF)

- **Funders:**
- NIEHS
- URMC EHSC and IHSFC
- BIRCWH program

And especially all of the study subjects and staff who made these studies possible!