Arsenic in Rice: Is this really a problem?

Mark Miller MD, MPH

PEHSU Annual Meeting, June 2017

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(Comments do not represent state of California)

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*Funded by Agency for Toxic Substances Disease Registry and US EPA through ACMT

No disclosures

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Objectives

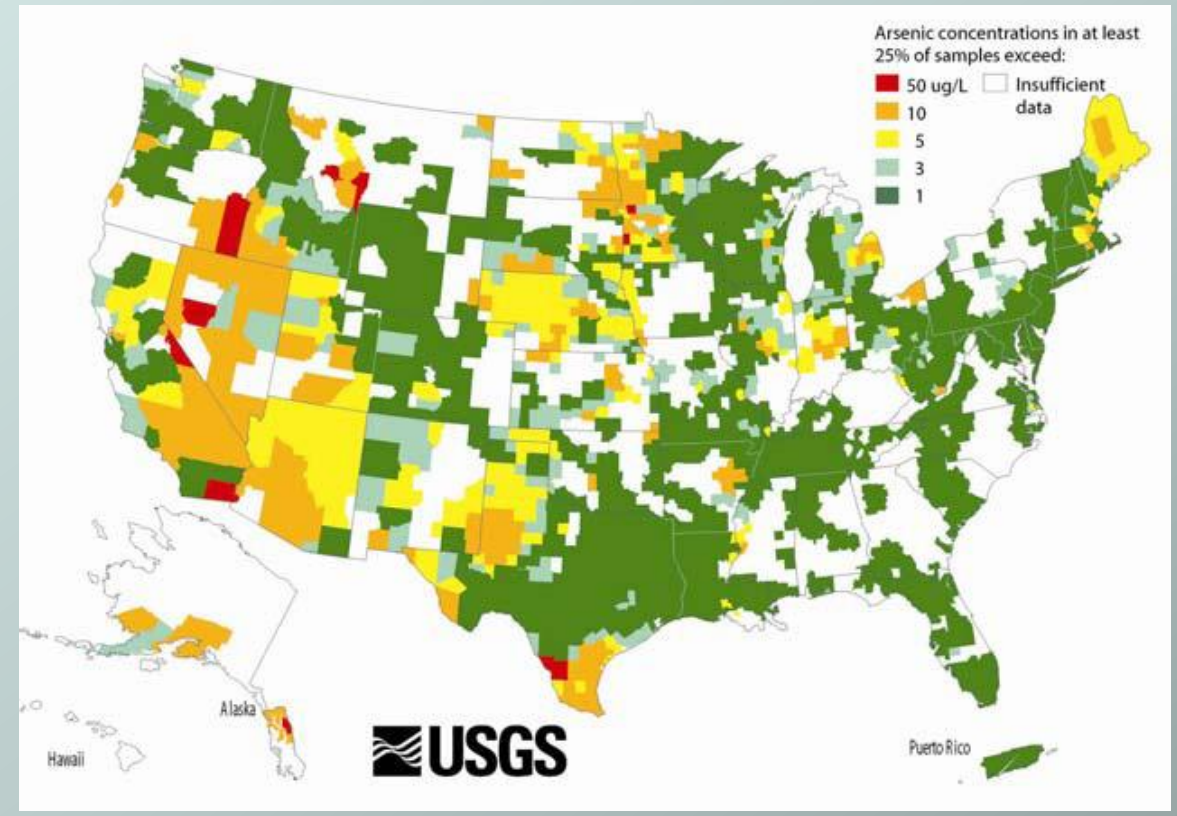
1) Participants will be able to identify key rice and rice products that contribute to As exposure burdens of pregnant women, infants and children.

2) Identify at least 3 groups of people at higher risk for exposure to As from rice.

3) Be able to put into context for concerned parents the risks associated with As exposure from rice.

4) Identify rice types and cooking methods associated with least As exposure.

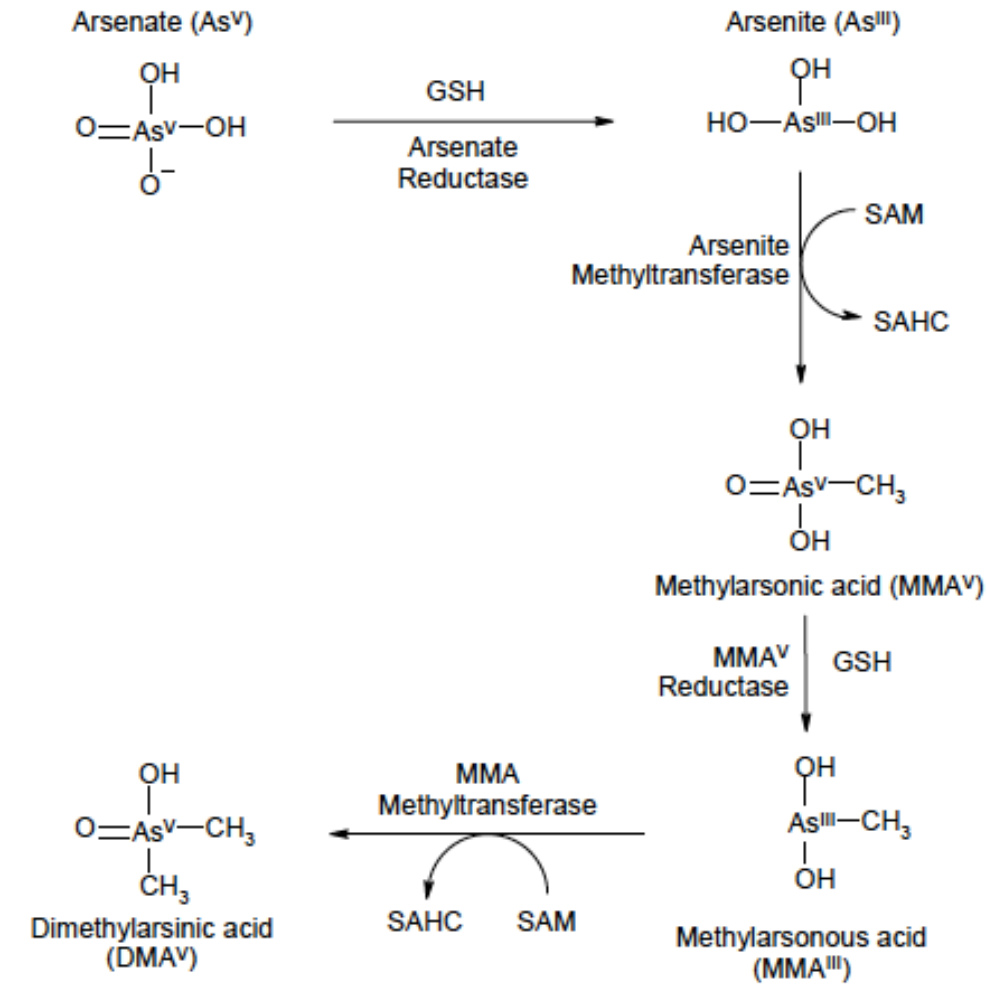
As in water still an issue in the US



iAs metabolized to MMA and DMA

Toxicologic Profile Arsenic
ATSDR 2007

Figure 3-7. Inorganic Arsenic Biotransformation Pathway



SAHC = S-adenosylhomocysteine; SAM = S-adenosylmethionine

Source: adapted from Aposhian et al. 2000b

Rice is unique in ability to incorporate inorganic As

Part of the image collection of the International Rice Research Inst. Creative Commons

Rice Arsenic Varies by Location of Production

and varies significantly within regions

Origin	Mean total inorganic As		Min/Max total inorganic As	
	ppb	µgm/serving	ppb	µgm/serving
California*	43.1	1.9	27-56	1.2-2.5
India/Pakistan*	52.9	2.4	21-144	1.0-6.5
Arkansas/Texas	79.3	3.6	40-107	1.8-4.8
U.S.	94.3	4.2	77-112	3.5-5.1
*Values significantly different from others				

Analysis of Arsenic in Rice and other Grains, Food Safety and Sustainability Center
Consumers Reports 2014

Concentration of inorganic As in Rice measured by FDA

Type	N	Inorganic As (mean-ppb)	Inorganic As (range ppb)
Brown Basmati	13	122.7	66-200
Brown Jasmine	2	132.5	114-151
Brown Long/Short	98	160.5	34-249
White Basmati	40	61.8	20-144
White Jasmine	11	78.4	34-110
White Long	148	103.3	23-196

Adapted from table 4.2 - Arsenic in Rice and Rice Products Risk Assessment Report, FDA 2016

Alternative grains - 1/10th the As

Table 10: Alternative Grains

Type	Mean Total Inorganic Arsenic		Min-Max Total Inorganic Arsenic	
	ppb	mcg/serving	ppb	mcg/serving
Amaranth[GF]	6.2	0.28	3.8-11.3	0.17-0.51
Barley	10.4	0.47	1.9-20.8	0.09-0.94
Buckwheat[GF]	5.6	0.25	3.8-7.4	0.17-0.33
Bulgar	8.4	0.38	4.8-16.7	0.22-0.75
Farro	7.3	0.33	2.0-10.1	0.09-0.45
Millet[GF]	12.1	0.54	6.4-26.8	0.29-1.21
Polenta/Grits[GF]	4.2	0.19	1.9-5.4	0.09-0.24
Quinoa[GF]	12.5	0.56	2.6-35.5	0.12-1.60

Arsenic in Rice and Rice Products Risk Assessment Report, FDA 2016

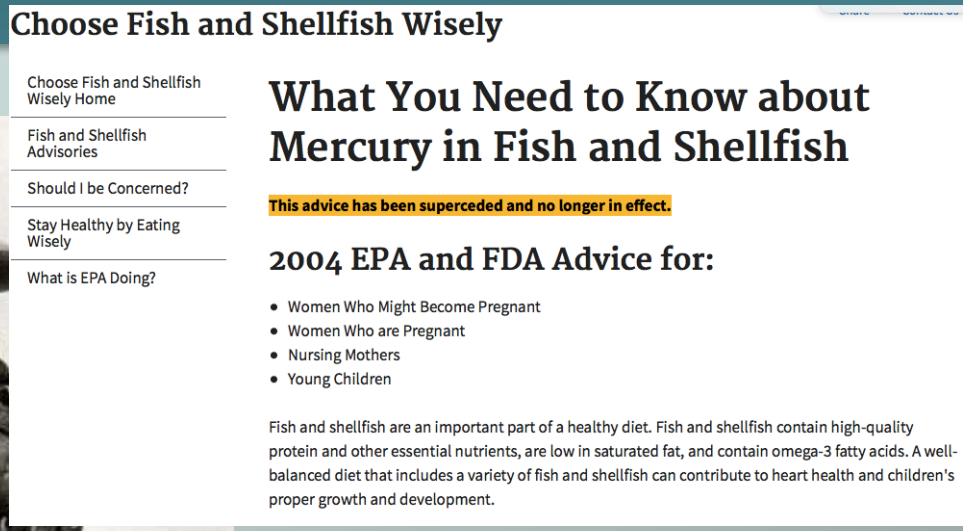
Dewi Sri – Indonesian rice goddess

Phosop – Thailand
Po Ino Nogar – Cambodia
Nang Khosop - Laos

History of rice cultivation
- interdependant culture

Wheat cultivation
- independant

Tropenmuseum, part of the National Museum of World Cultures [CC BY-SA 3.0 (http://creativecommons.org/licenses/by-sa/3.0)], via Wikimedia Commons



Choose Fish and Shellfish Wisely

Choose Fish and Shellfish Wisely Home
Fish and Shellfish Advisories
Should I be Concerned?
Stay Healthy by Eating Wisely
What is EPA Doing?

What You Need to Know about Mercury in Fish and Shellfish

This advice has been superceded and no longer in effect.

2004 EPA and FDA Advice for:

- Women Who Might Become Pregnant
- Women Who are Pregnant
- Nursing Mothers
- Young Children

Fish and shellfish are an important part of a healthy diet. Fish and shellfish contain high-quality protein and other essential nutrients, are low in saturated fat, and contain omega-3 fatty acids. A well-balanced diet that includes a variety of fish and shellfish can contribute to heart health and children's proper growth and development.

Adverse Health Effects from Arsenic Exposure

Organ System	Effects
Skin	Keratosis, Melanosis
	Skin Cancer
Neuro	Impaired intellectual function
	Impaired motor function
	Peripheral neuropathy
Respiratory	Pulmonary tuberculosis
	Bronchiectasis
	Lung cancer
	Lower Respiratory Tract Infections
	Decreased lung function
Cardiovascular	Coronary/ischemic heart disease
	Acute myocardial infarction
	Hypertension
Gastrointestinal	Liver cancer
Renal	Kidney cancer
Genitourinary	Bladder cancer
Reproductive	Low birth weight

Low dose exposure studies are proliferating

Fetal immune function (*in utero* exposure)

- Changes in CD4+/CD8+ ratios in cord blood
- IL1β levels positively related to As

IQ - >5 vs. <5 µgm/L

- 5-6 full scale points loss

Diabetes (adults)

- Gestational Diabetes

Respiratory infection

- In Utero exposure related to increases wheezing, meds, etc.
  during 1st year

Nadeau et al., Clinical Imm 2014; Wasserman et. al., Env Res 2014; Brauner et al., Env Health Persp. 2014; Shapiro et. al., Env Int. 2015; Farzan et al., EHP 2015

Early life exposure: greater lung and bladder cancer risk

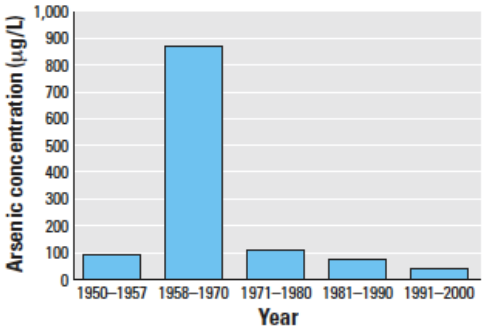
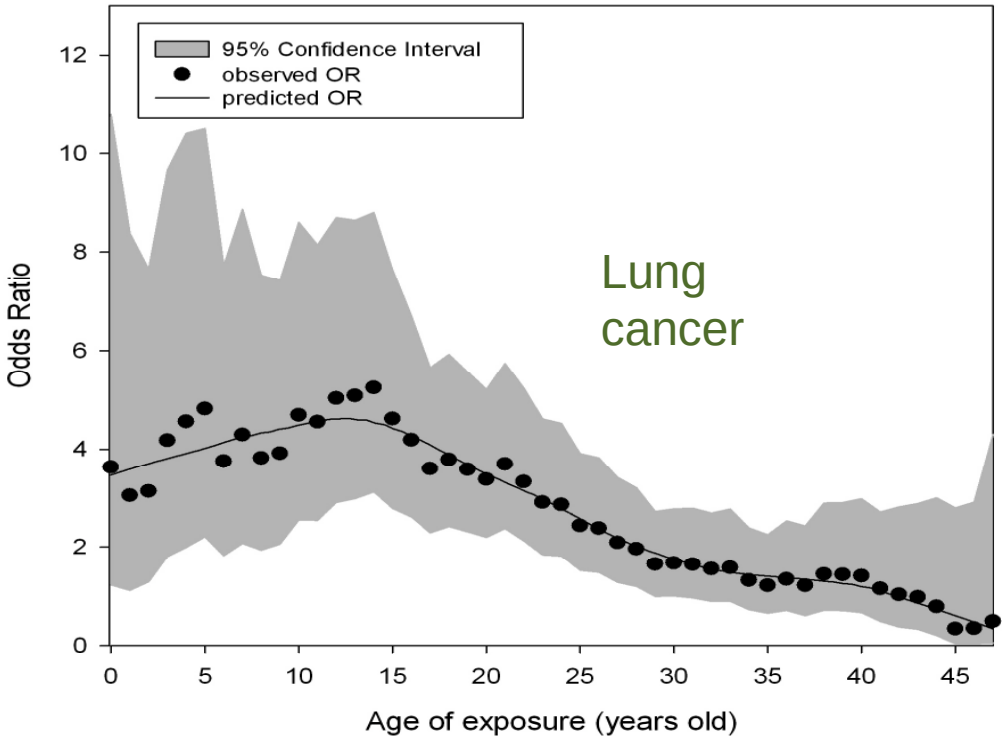
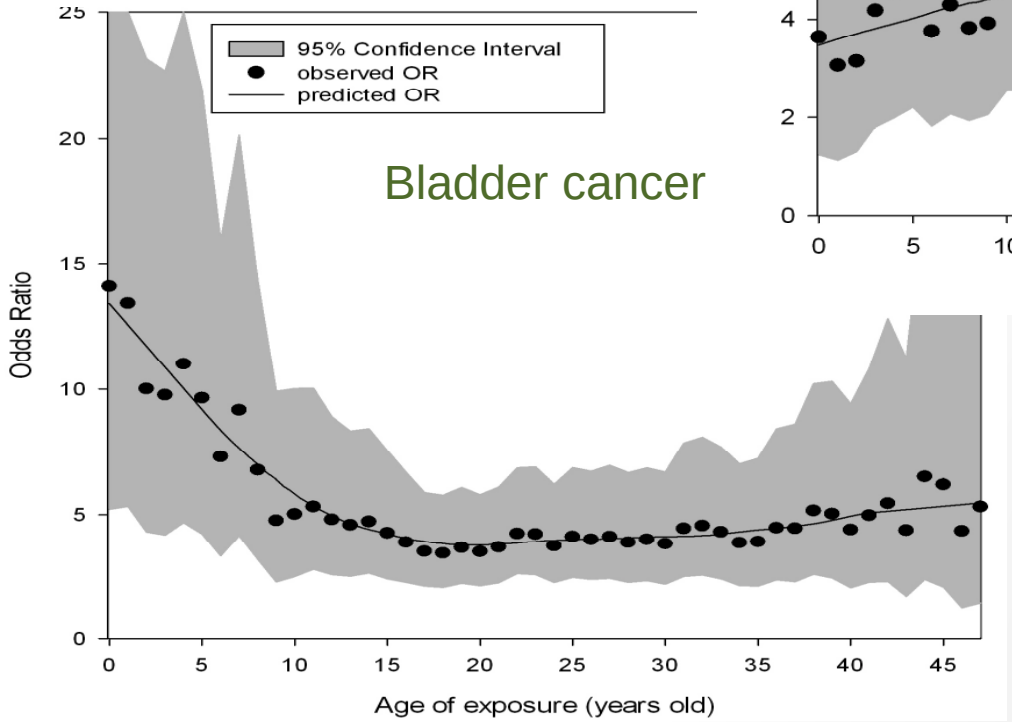


Figure 1. Arsenic concentrations in Antofagasta/Mejillones water by year. An arsenic removal plant was installed in 1971.





Craig Steinmaus
From Lai et. al. J Peds 2015

US Water Standard

10 µg As/L x 1L/day (adult) = 10 µg/d

10 µg/d results in excess cancer risk 1 in 300 *

- Eating 0.56 cups of cooked rice/d

= as much as 10 µg/d**

Top 1% rice-eating children eat ≥ 1.75 cups

= >> 1 in 300 estimated cancer risk

*National Academy of Sciences 2001

**Gilbert-Diamond et al. Rice consumption contributes to arsenic exposure in US women PNAS 2011

Rice containing foods (iAs per serving)

Average levels of inorganic arsenic

Product	Inorganic arsenic (mcg/serving)
Bakery mixes and pudding	4.1
Beverages (incl. protein and rice drinks, beer)	2
Cereals	2.6
Grain-based bars	1.8
Rice cakes	4.3
White rice	4.2
Brown rice	7.2
Basmati rice	3.5

Brief summary of rice grain and rice products sampled by the FDA and the corresponding amount of inorganic arsenic per serving, based on data published in 2013 (FDA and Consumers Reports).

Rice Consumption Associated with Risk of Skin Lesions

OPEN ACCESS Freely available online

PLOS ONE

Urinary and Dietary Analysis of 18,470 Bangladeshis Reveal a Correlation of Rice Consumption with Arsenic Exposure and Toxicity

Stephanie Melkonian[1], Maria Argos[1], Megan N. Hall[2], Yu Chen[4], Faruque Parvez[2], Brandon Pierce[1], Hongyuan Cao[1], Briseis Aschebrook-Kilfoy[1], Alauddin Ahmed[5], Tariqul Islam[5], Vesna Slavcovich[3], Mary Gamble[3], Parvez I. Haris[6], Joseph H. Graziano[2,3], Habibul Ahsan[1,7*]

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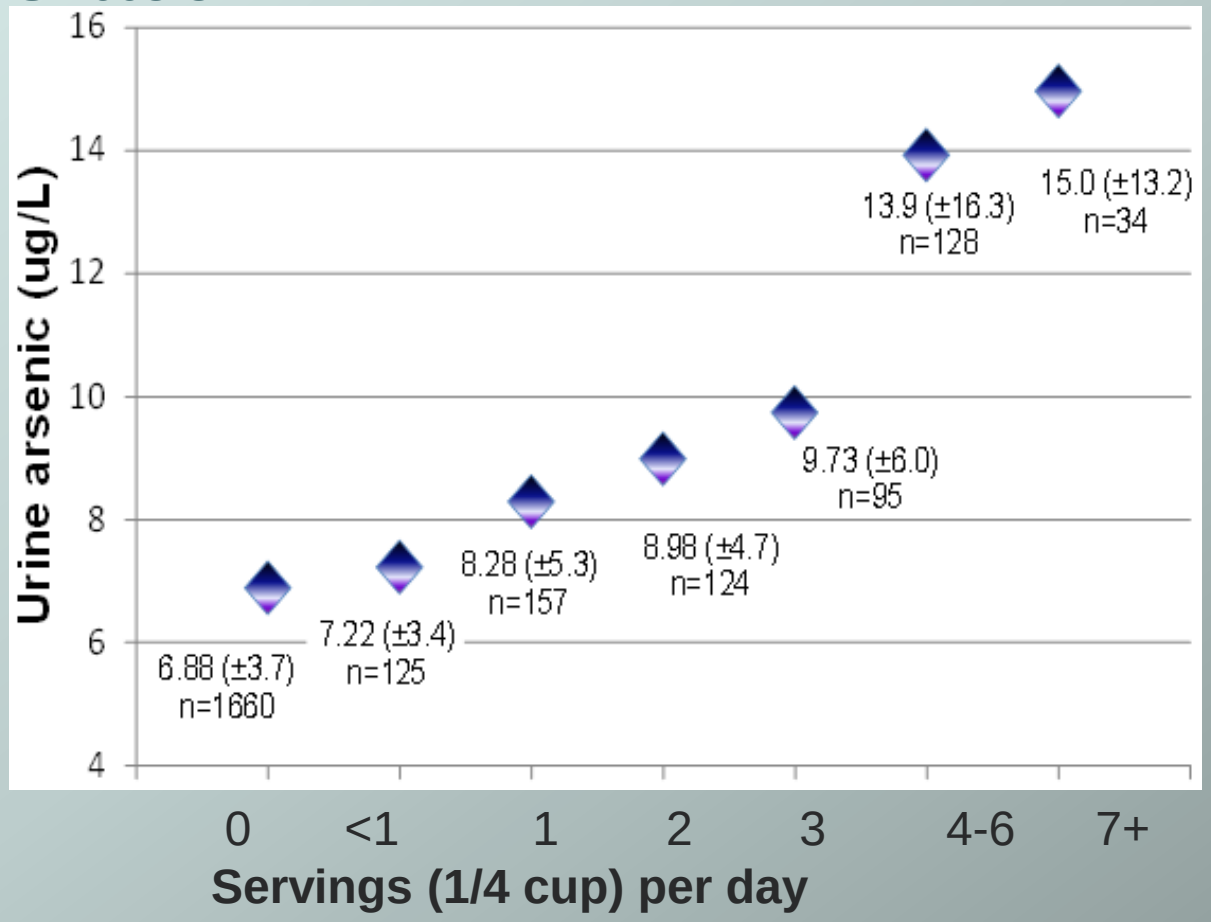
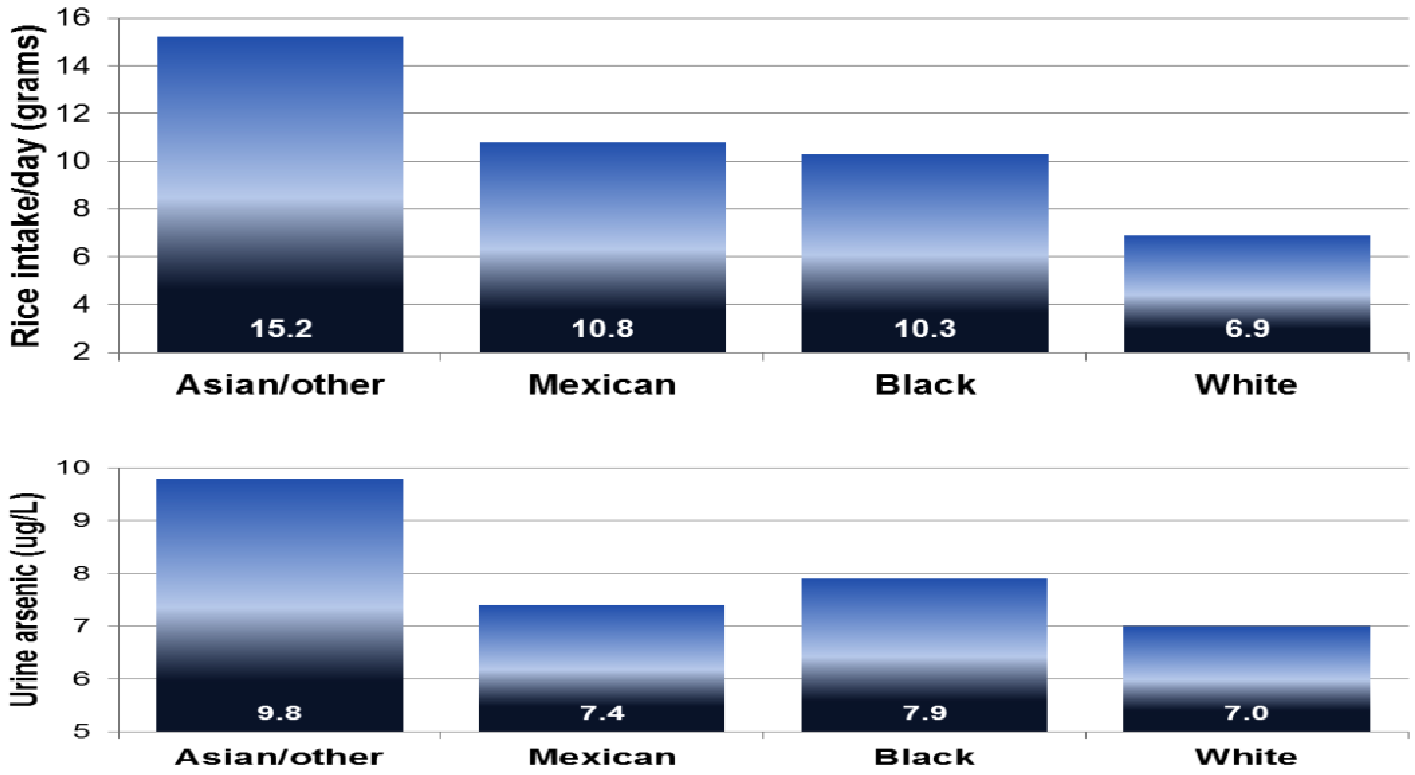
Increasing rice intake in children associated with urinary arsenic excretion

Increasing median urine arsenic with increasing rice intake in children, NHANES 2003-8



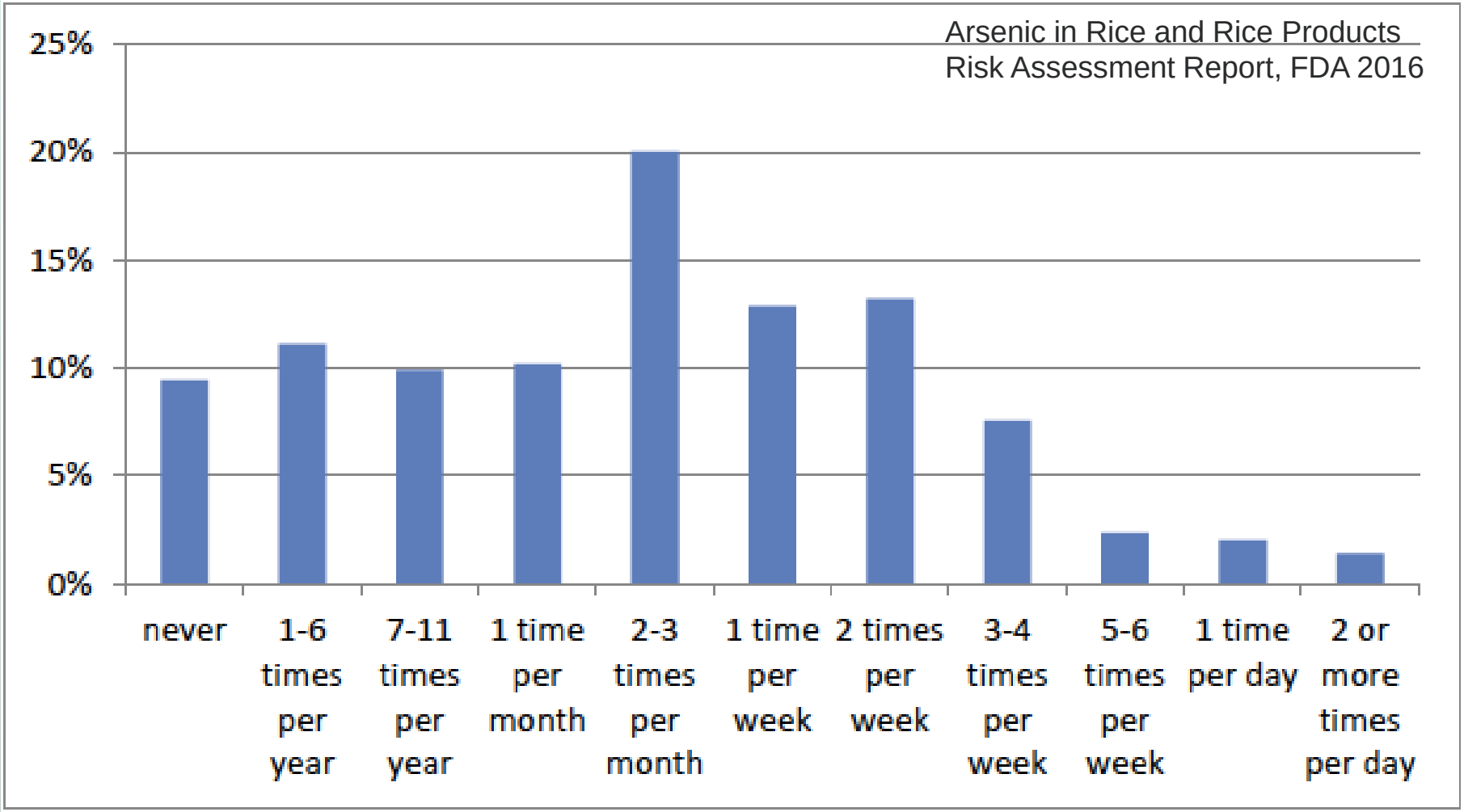
Adapted Lai et. al. J Peds 2015

Figure 4. Urinary arsenic and rice intake levels in children by race, NHANES 2003-8



Courtesy Craig Steinmaus, OEHHA, CA EPA
Lai et. al., J Peds 2015

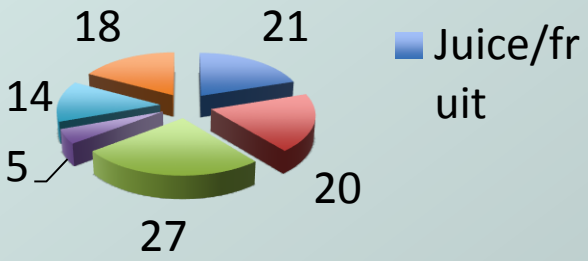
How often do you eat rice or other cooked grains?



Rice predominates as dietary source for high end childhood As consumers

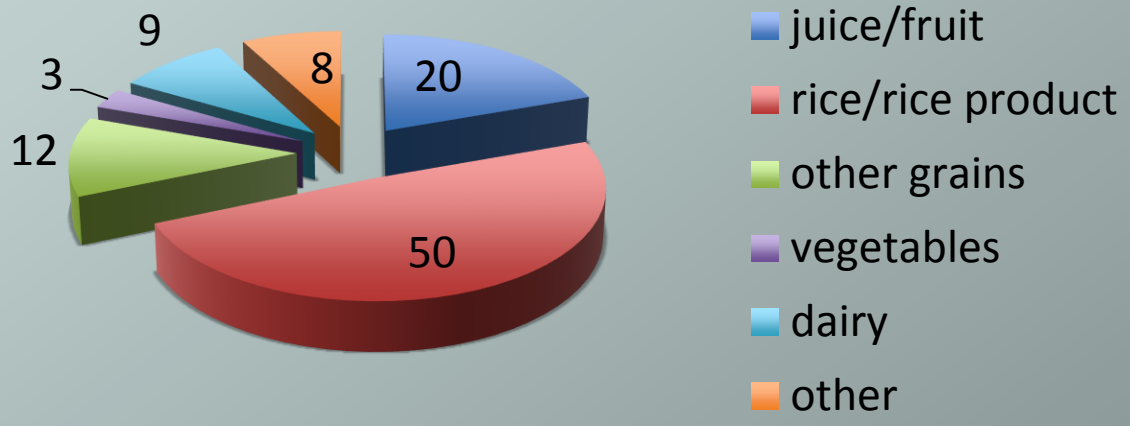
based on USDA food consumption data and modeling

percent dietary contribution (mean intake)



percent dietary contribution

95 % intake



Based on data from Yost et. al. Human and Ecologic Risk Ass. 2004

Who are at risk?

- Children / Infants
- High rice consumers
  - Asian American and others with tradition of rice based diet
  - Poor
  - Celiac disease / Gluten Free Diets
  - Food allergies
  - Macrobiotic Diet

FDA announces draft guidance on arsenic in rice
April 2016

Maintain infant rice cereal below As 100 ppb

- Proposed regulatory limit

Same dietary guidance as previous

- Rice cereal should not be sole source of supplementation for infants
- Everyone should eat a varied diet

Further study

- EU standard for rice destined for use in products for infants and young children 0.1 mcg/kg

Commission Regulation (EU) 2015/1006 of 25 June 2015 amending Regulation (EC) No 1881/2006 as regards maximum levels of inorganic arsenic in foodstuffs

Rice Type (uncooked/unprepared)	n	Inorganic Arsenic Mean Concentration[a,b] (ppb[c])	Inorganic Arsenic SEM[d] (ppb)	Range of Inorganic Arsenic Concentration (ppb)
White Medium grain, regular	91	80.9	2.6	39 – 174
White Short grain, regular	23	78.9	3.5	52 – 102
Infant Brown Rice Cereal	59	119.9	6.4	30 – 254
Infant White Rice Cereal	86	105.3	2.2	21 – 151

[a] Data source: FDA (2013) and FDA (2016).

[b] Arithmetic mean. For one brown and one white basmati rice sample, inorganic arsenic concentration was imputed as half of the total As.

[c] ppb = µg/kg or ng/g

Arsenic in Rice and Rice Products Risk Assessment Report, FDA 2016

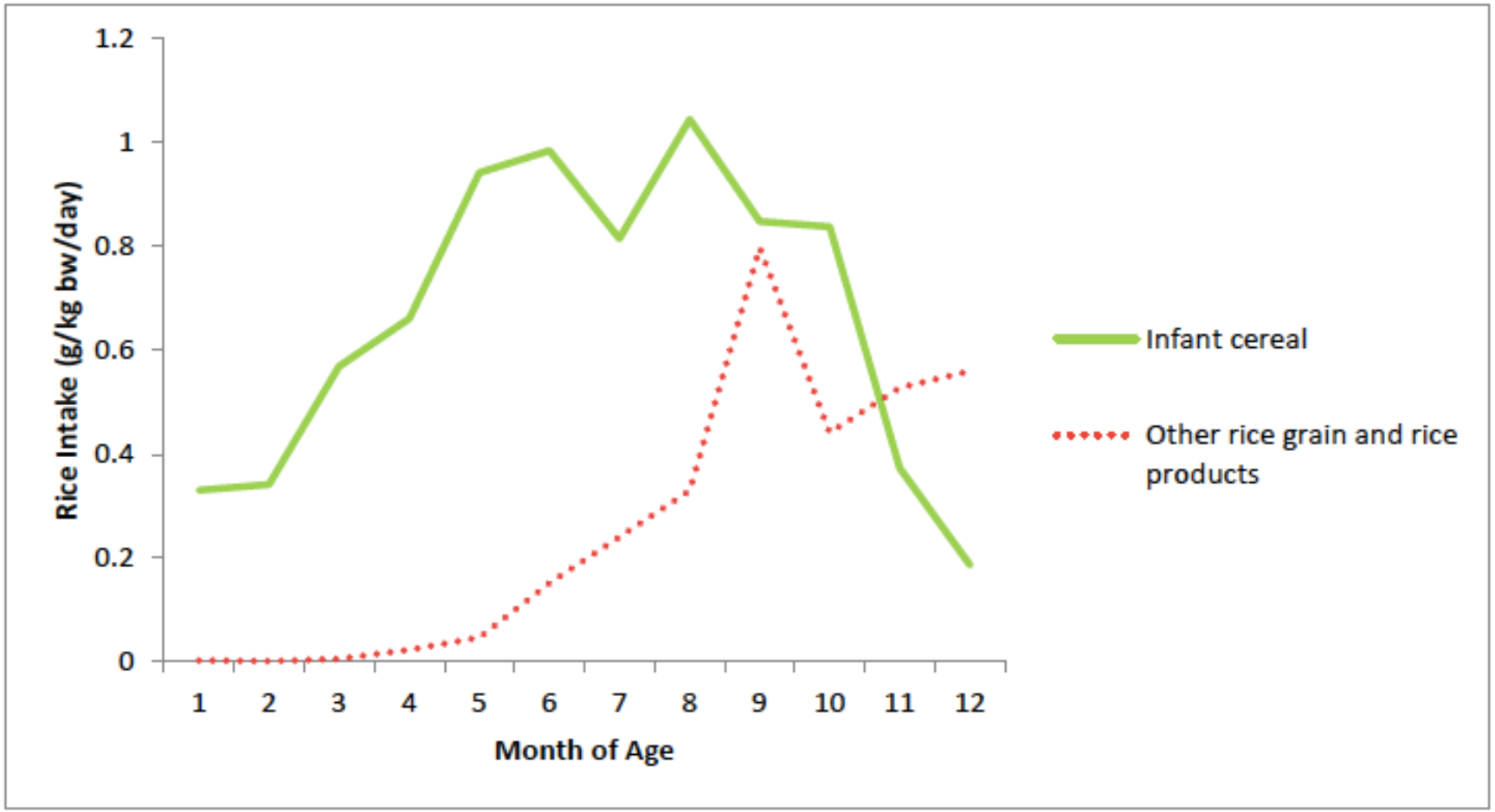


Figure 4.2. Intake of Infant-Rice Cereal and Other Rice Grain and Rice Products by Children 0 – 12 Months of Age

Data source: National Health and Nutrition Examination Survey (NHANES), What We Eat In America (WWEIA), 2003-2004, 2005-2006, 2007-2008, and 2009-2010. Food codes included in analysis are listed in Appendix 9.9.1. Mean rice intakes were estimated using NHANES statistical weights developed for the 2-day dietary data, to correct for differences in population-response rates. The body weight of each NHANES respondent was used to convert his/her intake in g/day to intake in g/kg bw/day.

Arsenic in Rice and Rice Products Risk Assessment Report, FDA 2016

Comparative intake by age

Arsenic in Rice and Rice Products Risk Assessment Report, FDA 2016

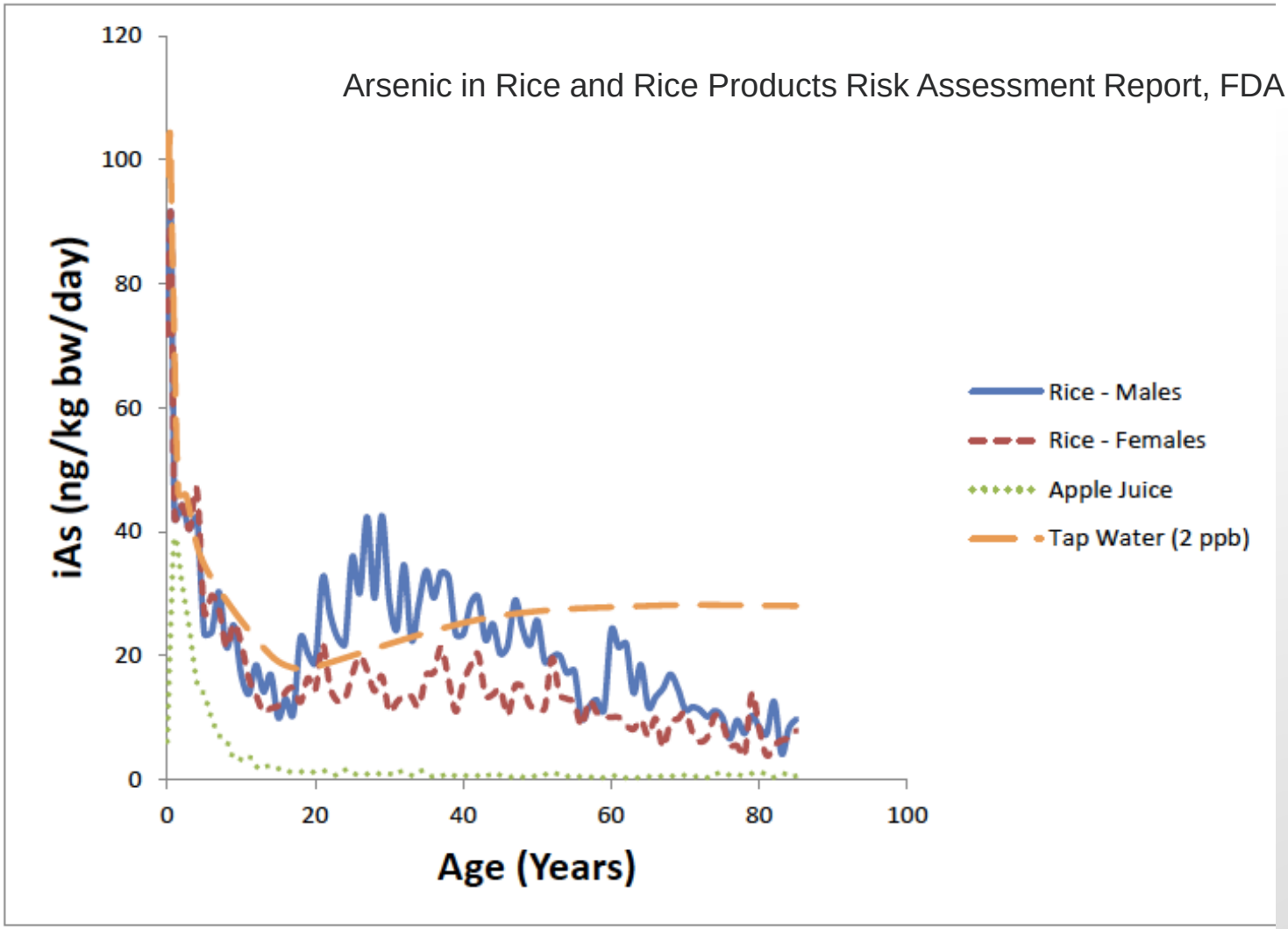


Figure 4.6. Mean per Capita Daily Inorganic Arsenic Intake from Rice (Grain and Products), Apple Juice, and Tap Water, by Age and Gender

Data source for inorganic arsenic (iAs) concentrations: FDA (2013) and Consumer Reports (2012).
Data source for rice and apple juice consumption estimates: National Health and Nutrition Examination Survey

Establishing limits

Table 5.4. Estimated Percentage of Market Above Specified Limit (in %)

Rice Type	200 ppb	150 ppb	100 ppb	75 ppb	50 ppb
Brown, Basmati	6	25	75	94	100
Brown, Infant Cereal	7.7	24.6	53.8	84.6	95.4
Brown, Long/Medium/Short grain	15.8	55.8	93.3	99.2	99.2
White, Basmati	0	0	10.3	21.2	46.3
White, Infant Cereal	0	1.1	62.0	91.3	98.9

Table 5.6. Percentage Risk Reduction from a Variety of Mandatory or Voluntary Limits (in %)

Rice Type	200 ppb	150 ppb	100 ppb	75 ppb	50 ppb
Brown, Basmati	4	17	39	51	N/A
Brown, Infant Cereal	11	21	37	54	68
Brown, Long/Medium/Short grain	7.8	22.6	47.3	78.5	78.5
White, Basmati	0	0	9	21	35
White, Infant Cereal	0	0	18.8	41.3	79.4

Arsenic in Rice and Rice Products Risk Assessment Report, FDA 2016

Table 5.9. Impact of Frequency and Amount Consumed on Predicted Total Lifetime Cancer Risks Attributable to Inorganic Arsenic in Rice and Rice Products (in Median Estimated Total Cancer Cases Per Million)

Rice Consumption Frequency	Infants[a,b] (< 1 year) Rice Cereal, White	Infants[a,b] (< 1 year) Rice Cereal, Brown	Children[a,b] (0 – 6 years)[c] White, Long Grain	Children[a,b] (0 – 6 years)[c] Brown[d]	Lifetime[a,b] (0 – 50 years)[c] White, Long Grain	Lifetime[a,b] (0 – 50 years)[c] Brown[d]
1 serving/day (baseline)	2.8	3.2	33	26	136	162
½ serving/day	1.4	1.6	17	13	68	81
3 servings/week	1.2	1.4	14	11	58	70
2 servings/day	5.6	6.3	66	52	272	330
3 servings/day	8.4	9.5	101	78	408	495

[a] All risk estimates are lifetime. The age range reflects the risk attributable to exposure during that interval.

[b] Values presented are the median number of cancer cases per million

[c] Amounts consumed per eating occasion ("serving") vary by age and rice type. Mean consumption by children (0 – 6 years) is 1.963 g/kg bw/eating occasion for white rice and 1.020 g/kg bw/eating occasion for brown rice; mean lifetime (0 – 50 years) consumption is 1.094 g/kg/eating occasion for white rice and 0.864 g/kg bw/eating occasion for brown rice.

[d] Long, medium-, and short-grain brown rice

Arsenic in Rice and Rice Products Risk Assessment Report, FDA 2016

Consumers Reports 2014 – point system

Food	Infant Cereal	Hot Cereal	Ready-to-Eat Cereal	Rice Drinks	Rice	Rice Pasta	Savory Rice Snacks	Rice Cakes
Serving Size	15 g	40 g	30 g	240 ml	45 g	55 g	30 g	30 g
Adult Points*	NA	3 1/2	2 1/4	2	3 1/2	3	1 1/4	2 1/2
Child Points*	1 1/4	8 1/4	4 1/2	-	5 1/2	7 1/4	2 3/4	6 1/4

*Calculations are for a child up to about 12 years of age (up to about 70 pounds) and an adult weighing 176 pounds, except for Infant Cereal recommendations, which apply only to infants (up to 1 year of age). Note: Point calculations are based on the 95th percentile levels of inorganic arsenic for each product category in the FDA data set.

Food	Cake & Muffin Mix	Brownie Mix	Pie & Pizza Crust	Pudding	Cookies	Sweet Rice Snacks	Cereal & Granola Bars	Energy Bars
Serving Size	55-80 g	40 g	40-55 g	30g	30 g	30 g	40 g	40 g
Adult Points*	1 1/2	1/2	1	3/4	3/4	1/2	1 1/4	1 1/4
Child Points*	3 3/4	1 1/4	2	1 3/4	1 3/4	1 1/4	2 3/4	2 3/4

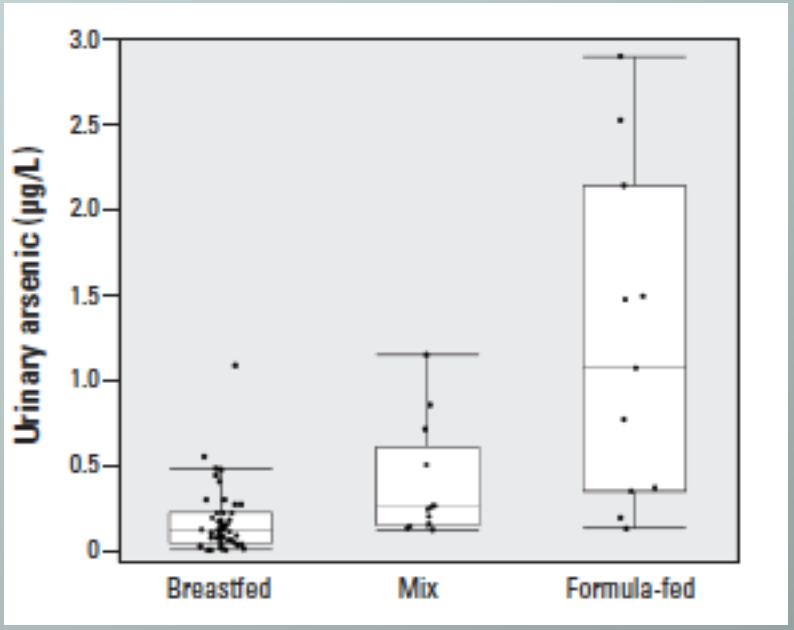
*Calculations are for a child up to about 12 years of age (up to about 70 pounds) and an adult weighing 176 pounds. Note: Point calculations are based on the 95th percentile levels of inorganic arsenic for each product category in the FDA data set.

http://www.consumerreports.org/cro/magazine/2015/01/how-much-arsenic-is-in-your-rice/index.htm

Arsenic readily crosses placenta

- Low birth weight
- Still birth
- Infant mortality

- BUT
  - Limited amount in breast milk even in areas with As in water

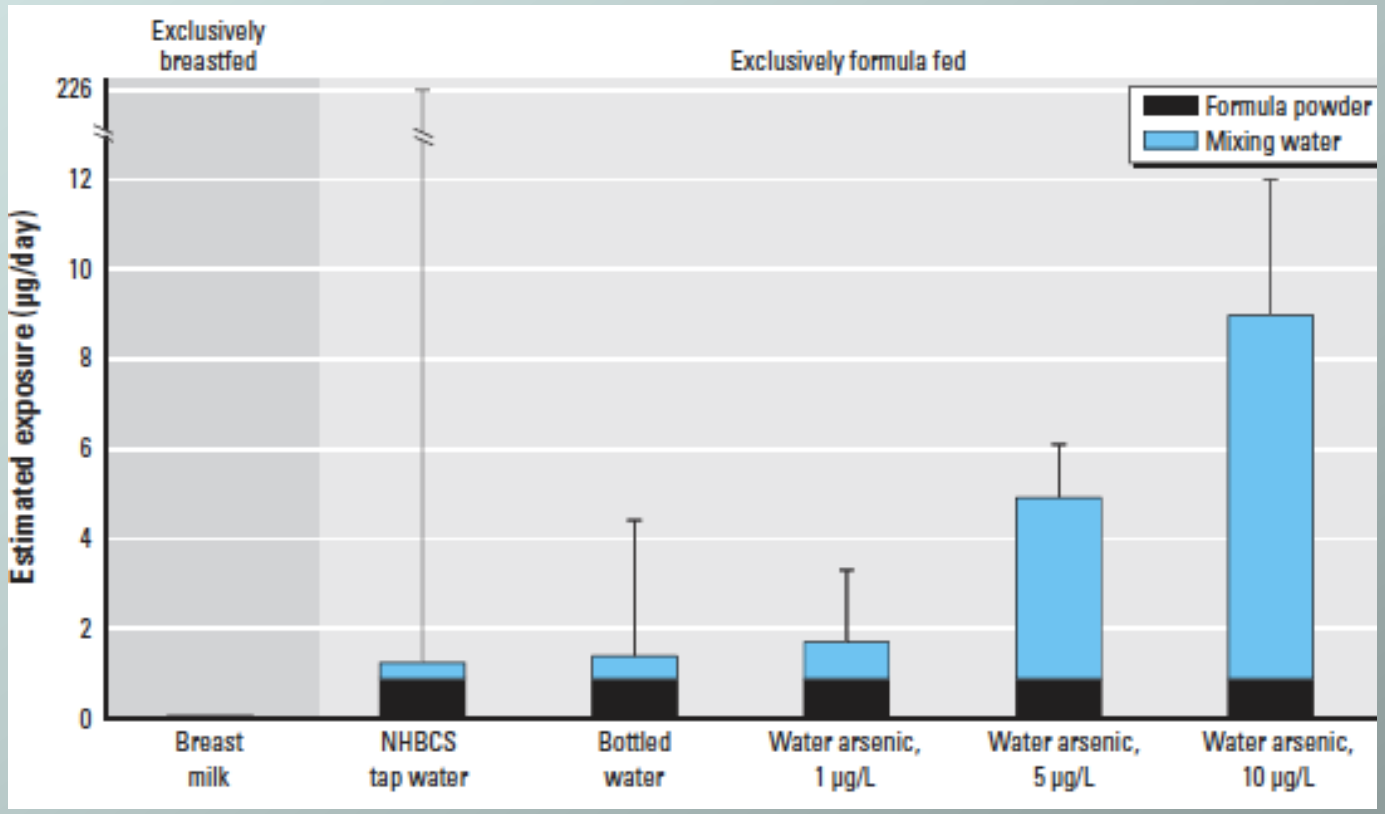


As by predominant feeding
Water As 2 ppb

Carignan et. al. EHP 2015

At low As water levels formula is significant contributor (70% of NHBCS median exposure)

Estimated As exposure for purely breastfed or formula fed 1-3 month olds US. Northeast



Carignan et. al. EHP 2015

What can I do?

- Choose varieties of rice lower in iAs
  - White over brown (nutrition tradeoffs)
  - Basmati, California/India/ Pakistan (caveats)
- Cooking method
  - Rinse and cook in excess water
    - 40-60% reduction, 70% reduction thiamine, Fe, folate, etc. (enriched rice)
- Limit number of servings
  - Consumers Reports point scale

Special messages for children

- Minimize use of infant rice cereal
  - Use alternative grains
- Rare use of rice beverages, rice pasta, and hot rice cereals in children
  - Gluten free, allergic
- Avoid products with rice syrup sweeteners
- Encourage breast feeding

Target High Consumers?

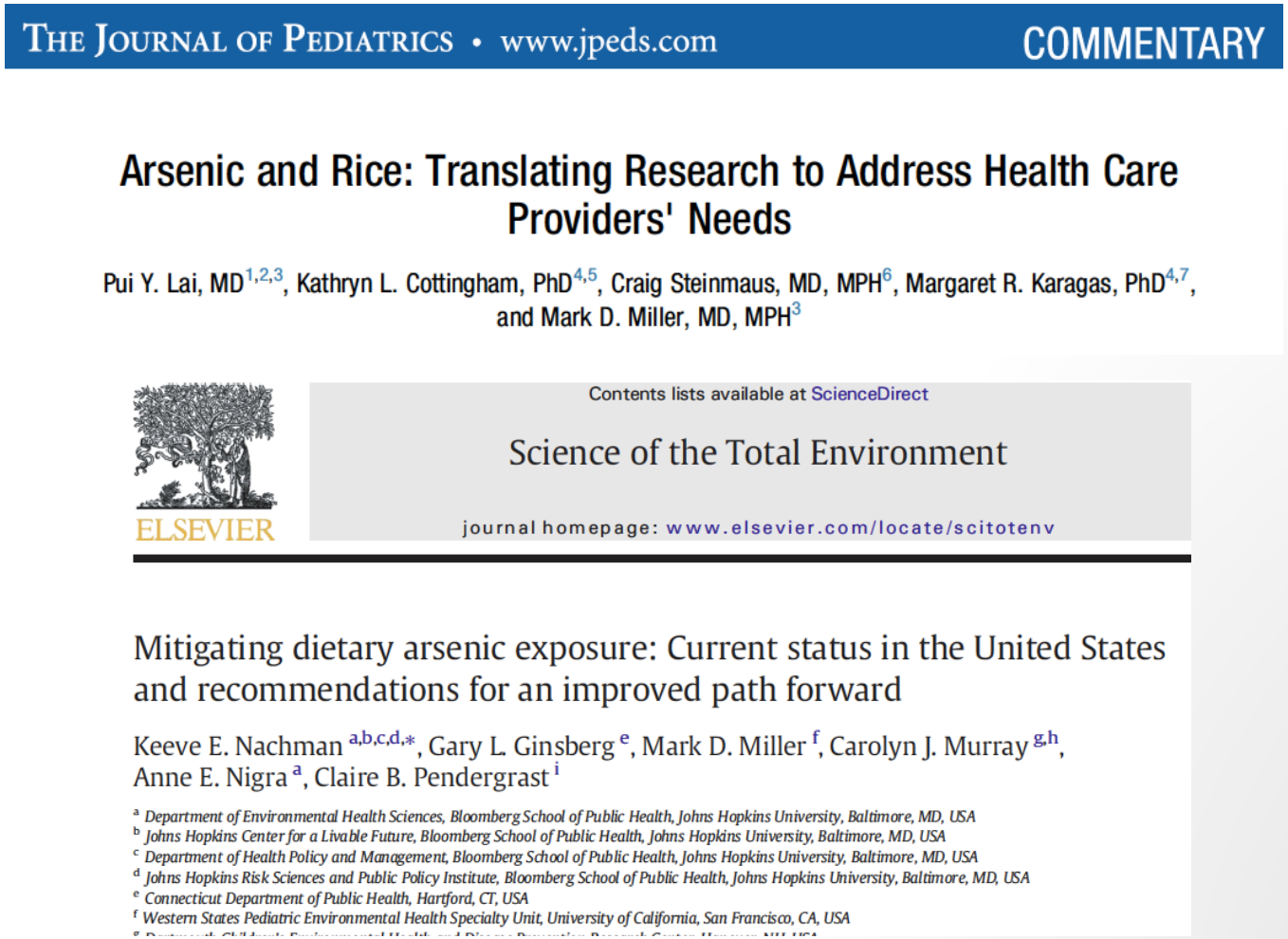
- High rice consumers
  - Asian American and others with tradition of rice based diet
  - Poor
  - Celiac disease / Gluten Free Diets
  - Food allergies
  - Macrobiotic Diet

Regulatory actions

- Does not fit traditional “Health Based” regulatory scheme
- Establish mandatory or voluntary limits
  - “Best Methods” limits (beyond infant cereal) that over time could decrease?
  - Labeling requirements, monitoring “targets” met
- Programs to improve food production for foods not meeting minimum standards
- Risk communication – reliable info on sources and dietary alternatives

Acknowledgements

Andy Meharg, Consumers Reports



THE JOURNAL OF PEDIATRICS • www.jpeds.com COMMENTARY

Arsenic and Rice: Translating Research to Address Health Care Providers' Needs

Pui Y. Lai, MD[1,2,3], Kathryn L. Cottingham, PhD[4,5], Craig Steinmaus, MD, MPH[6], Margaret R. Karagas, PhD[4,7], and Mark D. Miller, MD, MPH[3]

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journal homepage: www.elsevier.com/locate/scitotenv

Mitigating dietary arsenic exposure: Current status in the United States and recommendations for an improved path forward

Keeve E. Nachman [a,b,c,d,*], Gary L. Ginsberg [e], Mark D. Miller [f], Carolyn J. Murray [g,h], Anne E. Nigra [a], Claire B. Pendergrast [i]

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[f] Western States Pediatric Environmental Health Specialty Unit, University of California, San Francisco, CA, USA

FDA
Center for Food Safety and Applied Nutrition

Arsenic in Rice and Rice Products
Risk Assessment Report

Center for Food Safety and Applied Nutrition
Food and Drug Administration
U.S. Department of Health and Human Services

March 2016
Version Released for Public Comment

Per- and Polyfluoroalkyl Substances (PFAS): Overview of Public Health Issues for Infants

Pediatric Environmental Health Specialty Units (PEHSU)
Annual Meeting, June 29, 2017
Denver, Colorado

Michelle Watters, MD, PhD, MPH
Western Branch Associate Director of Science (acting)
Division of Community Health Investigations, ATSDR

National Center for Environmental Health
Agency for Toxic Substances and Disease Registry

Objectives

At the end of this presentation, the participant should:

1. be able to describe what PFAS are and where they might be found;
2. understand the ways in which infants and young children can be exposed to PFAS; and
3. recognize challenges in addressing community concerns about infant exposures.

Overview

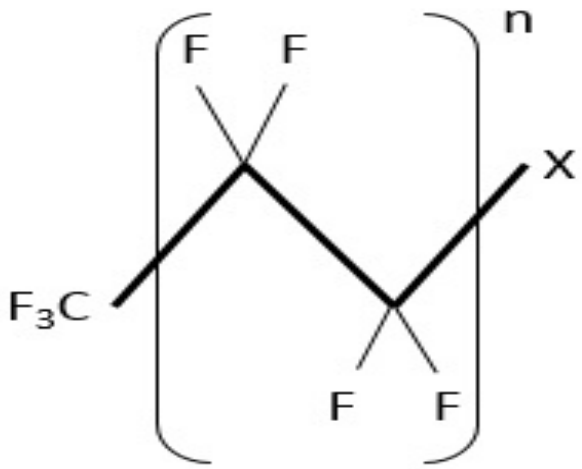
- What are PFAS?
- How can you be exposed to PFAS?
- What are the potential health effects from PFAS exposure?
- How does PFAS exposure affect infants?

WHAT ARE PERFLUOROALKYL AND POLYFLUOROALKYL SUBSTANCES (PFAS)?

What Are PFAS?

Manufactured chemicals consisting of a carbon chain surrounded by fluorine atoms and acid group (X).

- Carboxylic acid
- Sulfonic acid



Properties

- Water and oil repellent
- Surfactant, dispersant
- Persistent
- Some bioaccumulate

Shuiox rurrfwdqrlf dflg +SIRD,

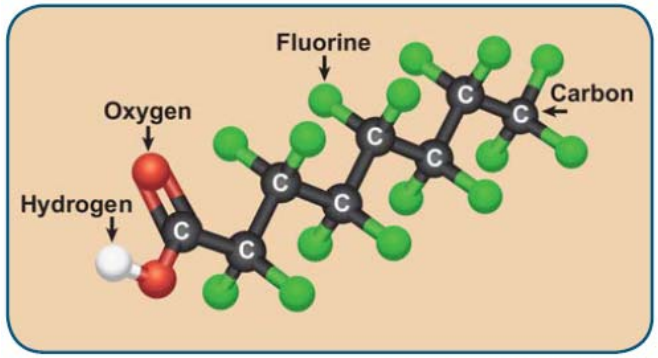
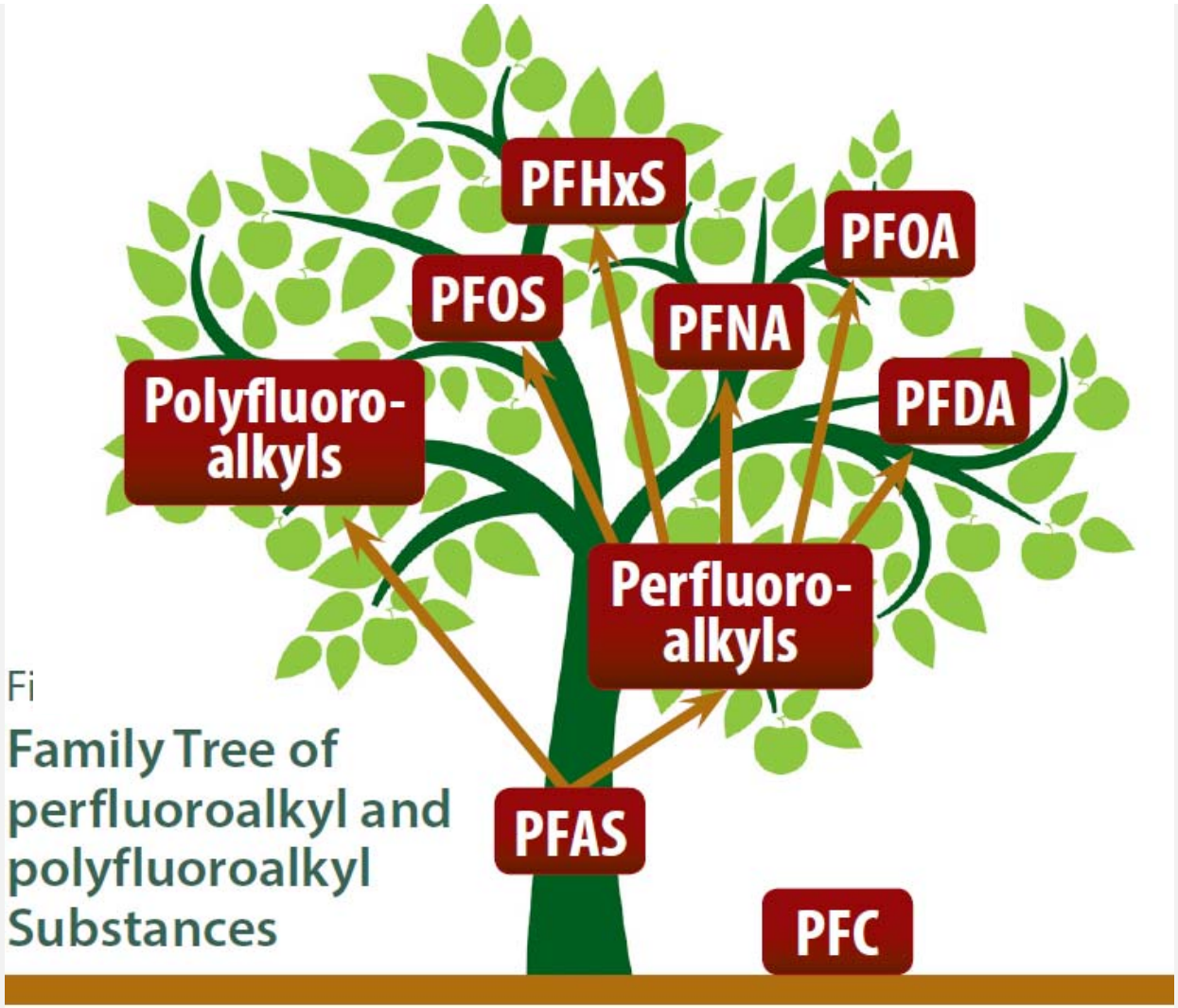


Image credit: NIEHS.



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Family Tree of perfluoroalkyl and polyfluoroalkyl Substances

Common PFAS: Abbreviations, Names, and Subfamilies

Abbreviation	Chemical Name	Other Name	Subfamily
PFOS	Perfluorooctane sulfonic acid		Perfluoroalkyl
PFOA	Perfluorooctanoic acid	C8	Perfluoroalkyl
PFNA	Perfluorononanoic acid		Perfluoroalkyl
PFDA	Perfluorodecanoic acid		Perfluoroalkyl
PFOSA	Perfluorooctane sulfonamide	FOSA	Polyfluoroalkyl
MeFOSAA	2-(N-Methyl-perfluorooctane sulfonamido) acetic acid	Me-PFOSA-AcOH	Polyfluoroalkyl
EtFOSAA	2-(N-Ethyl-perfluorooctane sulfonamide) acetic acid	Et-PFOSA-AcOH	Polyfluoroalkyl
PFHxS	Perfluorohexane sulfonic acid		Perfluoroalkyl

HOW CAN YOU BE EXPOSED TO PFAS?

Main uses of PFAS*

AFFF

carpets

fabrics

paints and stains

nonstick cookware

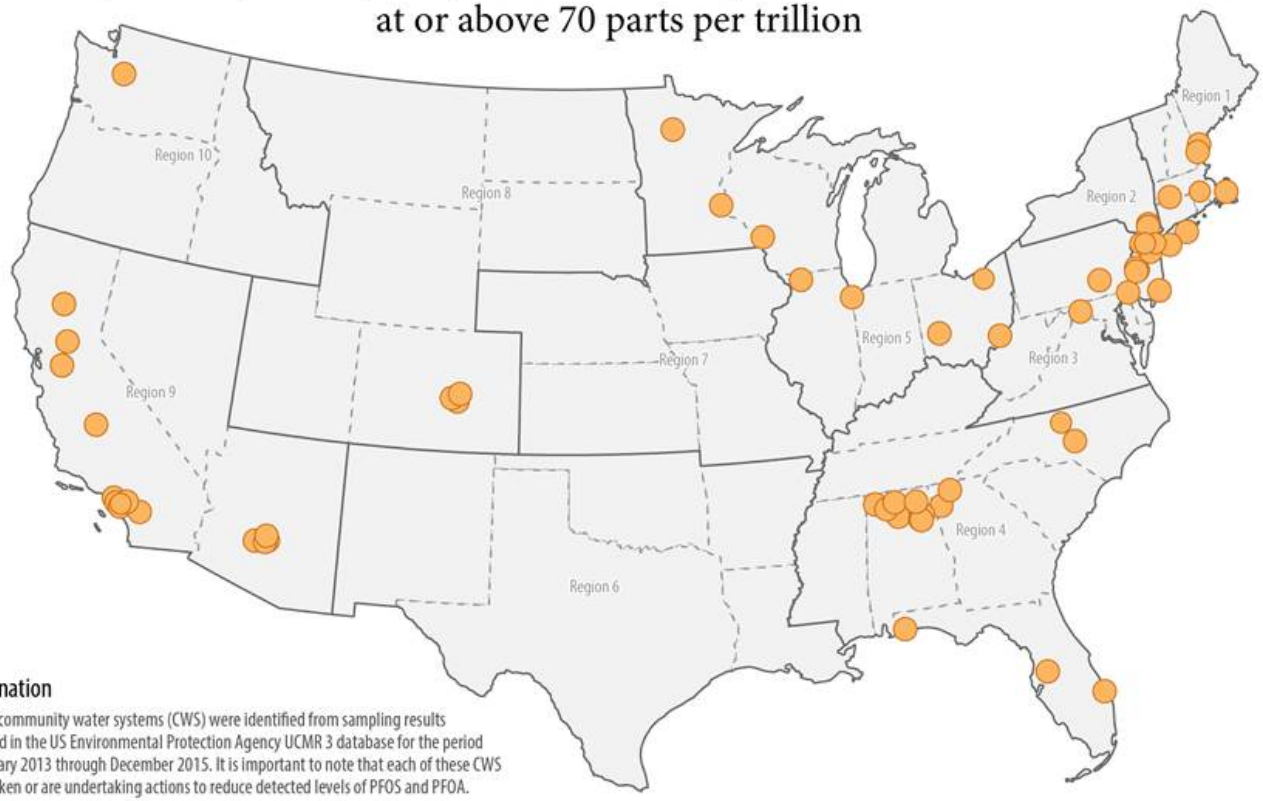
food packaging

*Note: Not all carpets, fabrics, food packaging, etc. contain PFAS.
AFFF: aqueous film-forming foam

Major non-occupational PFAS Exposure Pathways

- Drinking contaminated water
- Ingestion of contaminated food
- Incidental ingestion from hand-to-mouth transfer from surfaces treated with protectants containing PFAS

Community water systems (n=65) with UCMR3 reported levels of PFOS + PFOA (sum) at or above 70 parts per trillion



Explanation

The 65 community water systems (CWS) were identified from sampling results reported in the US Environmental Protection Agency UCMR 3 database for the period of January 2013 through December 2015. It is important to note that each of these CWS have taken or are undertaking actions to reduce detected levels of PFOS and PFOA.

Current and past community water systems (CWS) that reported PFOA+PFOS concentration at or above 70 part per trillion

PFOA, perfluorooctanoic acid
PFOS, perfluorooctane sulfonic acid
CWS, Community water system
UCMR, Unregulated Contaminant Monitoring Rule
ppt, parts per trillion

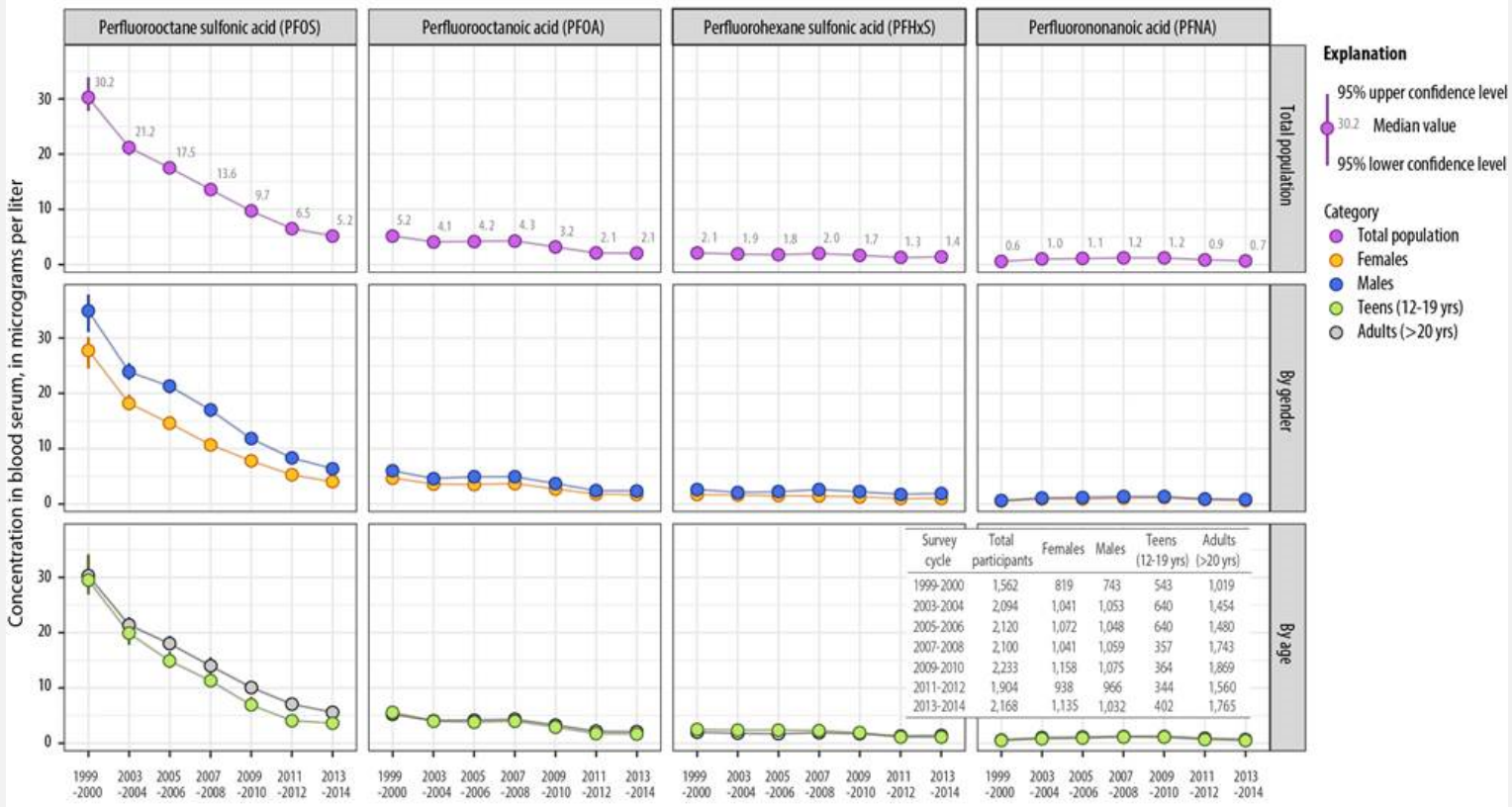
Not shown

- Community water system (CWS) in Guam
- CWS in Saipan, Northern Mariana Islands

Data source: USEPA UCMR 3 database (www.epa.gov/dwucmr/third-unregulated-contaminant-monitoring-rule) and ATSDR Regional staff.

Science Support Branch
data organization , analysis , visualization
Updated 2017.06.15 ATSDR/DCHI/SSB/ba

Median concentration of selected per- and polyfluoroalkyl substances (PFAS) in blood serum (1999-2014) in the United States



Survey cycle	Total participants	Females	Males	Teens (12-19 yrs)	Adults (>20 yrs)
1999-2000	1,562	819	743	543	1,019
2003-2004	2,094	1,041	1,053	640	1,454
2005-2006	2,120	1,072	1,048	640	1,480
2007-2008	2,100	1,041	1,059	357	1,743
2009-2010	2,233	1,158	1,075	364	1,869
2011-2012	1,904	938	966	344	1,560
2013-2014	2,168	1,135	1,032	402	1,765

Data source: Centers for Disease Control and Prevention. Fourth Report on Human Exposure to Environmental Chemicals, Updated Tables, (January 2017). Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention. https://www.cdc.gov/exposurereport/.

Note: In January 2006, the eight major PFAS manufacturing companies in the U.S. voluntarily committed to a 95% reduction of emissions and product content for PFOA and selected related PFAS species by 2010 and a complete elimination of these chemicals from emissions and products by 2015. At least one of these companies began reducing their production and use of these species in the early 2000s.

Science Support Branch

PFAS Exposure Assessment Technical Tools (PEATT)

PFAS Elimination in Humans

- Primarily eliminated in urine
- Factors that affect elimination rates
  - Sex
  - Concentration of serum proteins
  - Blood donation
  - Menstruation
  - Gestation
  - Lactation
- Shorter chain PFAS tend to be eliminated faster than long chain PFAS

Biological Half-life in Humans

Substance	Estimated Half-life
Perfluorooctanoic acid (PFOA)	2-4 years
Perfluorooctanesulfonic acid (PFOS)	5-6 years
Perfluorohexane sulfonic acid (PFHxS)	8-9 years
Perfluorobutane sulfonic acid (PFBS)	0.1 years

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WHAT ARE THE POTENTIAL HEALTH EFFECTS FROM PFAS EXPOSURE?

Animal Studies

- **Wide range of potential health endpoints**
  - Liver enlargement
  - Changes in serum lipid and cholesterol concentrations
  - Reduced body weight
  - Changes in thyroid hormone levels
  - Reduced testosterone synthesis
  - Suppression of antibody response
  - Tumor formation—pancreatic, hepatic, testicular

C8 (PFOA) Health Project

- **Exposure-** 1950s-2002**,** six water districts near Parkersburg, West Virginia
- **Data collected-** health and exposure data from class members of a lawsuit 69,030 adults (≥18 years of age) from 2005-2013

- **Probable Link***
  - Thyroid disease (potential to affect T4 and TSH levels)
  - High cholesterol
  - Pregnancy-induced hypertension
  - Ulcerative colitis
  - Testicular cancer
  - Kidney cancer

* A "probable link" in this setting is defined in the Settlement Agreement to mean that given the available scientific evidence, it is more likely than not that among class members a connection exists between PFOA exposure and a particular human disease.

Some Limitations of C8 Results

- Thyroid Disease
  - Subclinical measures (TSH, free thyroxine index)
  - Lack of coherence among studies (high and low measurements)
- High Cholesterol
  - The majority of epidemiological studies demonstrated strong associations between serum PFOA and PFOS concentrations and total cholesterol.
  - Other studies have found no association between PFAS exposures and the total cholesterol levels.
- Pregnancy-induced Hypertension and Pre-eclampsia
  - Review of birth records (PIH) and self-reporting (PE)
  - Potential confounding
  - Uncertainty regarding size of effect

Reproductive Effects

- Limited number of studies
- The Longitudinal Investigation of Fertility and the Environment (LIFE) study: evaluated PFAS and human semen quality
- Danish National Birth Cohort: evaluated PFAS plasma concentrations and fecundity
    - Longer time to pregnancy was associated with higher maternal concentrations of PFOA and PFOS in multiparous women.
- Further research is needed

PFOA/PFOS and Antibody Response

- There is strong evidence of antibody suppression with increased concentrations of both PFOA and PFOS in animal studies.
- Human studies suggest a similar pattern of reduced antibody response to specific vaccines with increasing concentrations of PFOA and PFOS.
  - Results were not consistent among studies for all vaccines
  - Reduced response demonstrated to rubella, diphtheria, mumps, and (for PFOA) tetanus vaccines
    - No evidence that these effects have resulted in an increased risk for diseases prevented by vaccines

NTP systematic review concluded that PFOA/PFOS is *presumed to be an immune hazard to humans.*

PFAS and Cancer

- International Agency for Research on Cancer (IARC) has classified PFOA as possibly carcinogenic
- EPA has concluded that both PFOA and PFOS are possibly carcinogenic to humans.
- Increased risk for certain types of cancer were found in communities and workers exposed to PFAS
- Studies:

  Bladder (=), Kidney (+), Pancreas (-), Prostate (=/+), Thyroid (=/+)

HOW DOES PFAS EXPOSURE AFFECT INFANTS?

Animal Studies

- **Developmental and reproductive effects**
  - Reduced birth weight
  - Decreased gestational length
  - Structural defects
  - Delays in postnatal growth and development
  - Increased neonatal mortality
  - Developmental and reproductive effects
  - Pregnancy loss

Pregnancy Outcomes

- Limited number of human studies
- Main outcomes assessed by studies:
  - Stillbirth
  - Preeclampsia
  - Preterm birth
  - Term low birthweight
  - Birth defects
- No consistent associations were observed between serum PFAS and the outcomes listed above

PFAS in Cord Blood

- Different trans-placental transfer rates
- Strong correlation between cord serum and maternal serum ($r^2 > 0.83$)

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PFAS in Breastmilk

- Breastmilk PFAS levels vary
- First nursed child has higher exposure than subsequently nursed children
- Breastfed infants can have higher serum levels than the mother

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Is it Safe to Breastfeed?

- Breastfeeding is associated with numerous health benefits for infants and mothers.
- At this time, it is recommended that a nursing mother continues to breastfeed her baby.
- The science on the health effects of PFAS for mothers and babies is evolving.
- However, given the scientific understanding at this time, the benefits of breastfeeding outweighs those of not breastfeeding.

Considerations when advising on breastfeeding

Healthy People 2020 Objectives	Target	Current Rates*
MICH-21:** Increase the proportion of infants who are breastfed		
MICH-21.1: Ever	81.9%	81.1%
MICH-21.2: At 6 months	60.6%	51.8%
MICH-21.3: At 1 year	34.1%	30.7%
MICH-21.4: Exclusively through 3 months	46.2%	44.4%
MICH-21.5: Exclusively through 6 months	25.5%	22.3%

*MICH-21 and MICH-23 current rates represent babies born in 2013, National Immunization Survey 2014-2015; MICH-24 current rates represent babies born in Baby-Friendly Hospitals and Birth Centers designated as of June 2016.
**Maternal Infant and Child Health

https://www.cdc.gov/breastfeeding/pdf/2016breastfeedingreportcard.pdf

Considerations when advising on breastfeeding

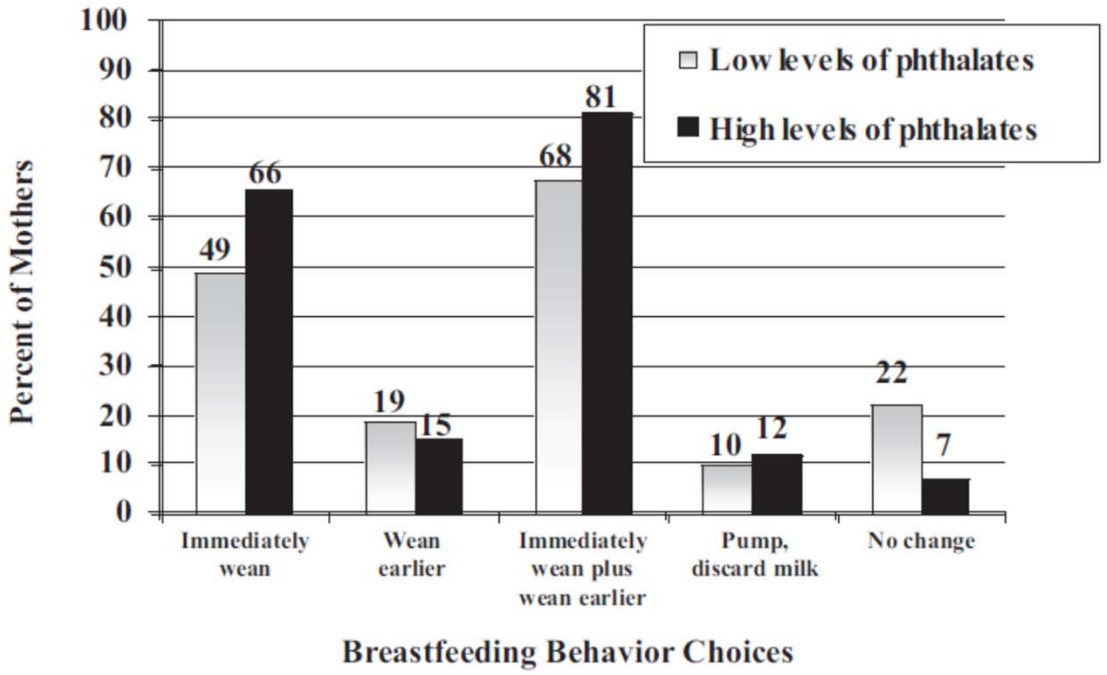


FIG. 1. Breastfeeding behavior choices of all breastfeeding mothers in the study when told they have low and high levels of phthalates in their breastmilk ($n = 196$).

Geraghty, et al. 2008 Breastfeeding Medicine 3(4);207-213.

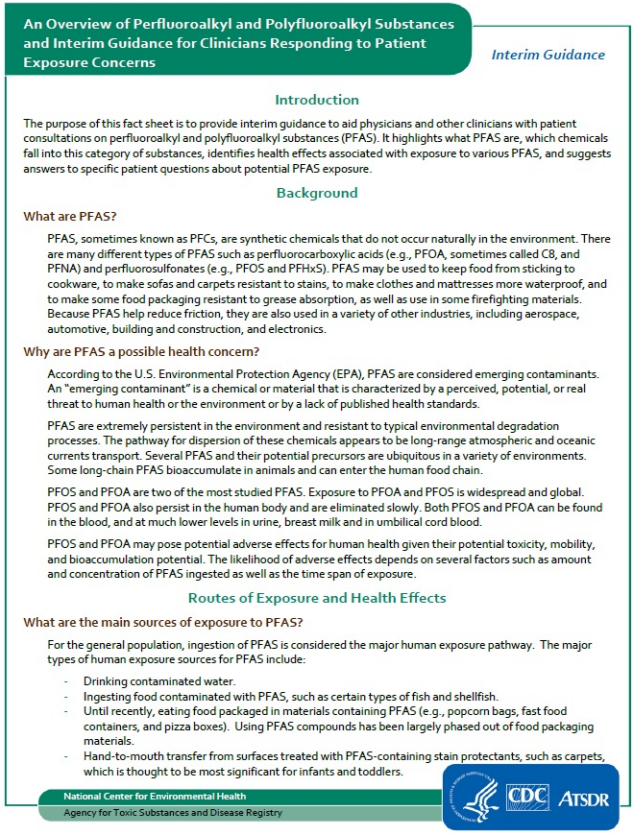
Breastfeeding and PFAS Reviews

- **AHRQ 2007: Breastfeeding and Maternal and Infant Health Outcomes in Developed Countries**
- **CDC/NCEH 2010: Breastfeeding and Lead**
  - Measurement of levels of lead in breast milk is not recommended.
  - Mothers with BLLs <40 µg/dL should begin breastfeed
  - Mothers with confirmed BLLs ≥40 µg/dL should begin breastfeeding when their blood lead levels drop below 40 µg/dL. Until then, they should pump and discard their breast milk.
- **USDA 2012-2018: Pregnancy and Birth to 24 Months Project**
  - Multiple systematic reviews on diet and health in infants, toddlers, and pregnant women
- **EPA funded 2014: PFOA and Fetal Growth**
  - Navigation guide systematic review methodology
  - "Sufficient" human evidence that developmental exposure to PFOA reduces fetal growth.
- **NTP 2016: PFOA/PFOS Immunotoxicity**
  - *Presumed to be an immune hazard to humans*
- **AHRQ 2017: Systematic Review of Breastfeeding Programs and Policies, Breastfeeding Uptake, and Maternal Health Outcomes in Developed Countries**

Additional Information

Resource	Link
ATSDR: PFAS portal	http://www.atsdr.cdc.gov/pfc/index.html
CDC/NCEH: NHANES	https://www.cdc.gov/exposurereport/index.html
C8 Science Panel	http://www.c8sciencepanel.org/prob_link.html http://www.c8sciencepanel.org/publications.html
EPA: PFAS	https://www.epa.gov/chemical-research/research-perfluorooctanoic-acid-pfoa-and-other-perfluorinated-chemicals-pfcs
IARC	http://www.iarc.fr/
NIEHS: PFAS	https://ntp.niehs.nih.gov/pubhealth/hat/noms/pfoa/index.html
Pediatric Environmental Health Specialty Units (PEHSU)	http://www.pehsu.net/

Patient Q & A



An Overview of Perfluoroalkyl and Polyfluoroalkyl Substances and Interim Guidance for Clinicians Responding to Patient Exposure Concerns

Interim Guidance

Introduction

The purpose of this fact sheet is to provide interim guidance to aid physicians and other clinicians with patient consultations on perfluoroalkyl and polyfluoroalkyl substances (PFAS). It highlights what PFAS are, which chemicals fall into this category of substances, identifies health effects associated with exposure to various PFAS, and suggests answers to specific patient questions about potential PFAS exposure.

Background

What are PFAS?

PFAS, sometimes known as PFCs, are synthetic chemicals that do not occur naturally in the environment. There are many different types of PFAS such as perfluorocarboxylic acids (e.g., PFOA, sometimes called C8, and PFNA) and perfluorosulfonates (e.g., PFOS and PFHxS). PFAS may be used to keep food from sticking to cookware, to make sofas and carpets resistant to stains, to make clothes and mattresses more waterproof, and to make some food packaging resistant to grease absorption, as well as use in some firefighting materials. Because PFAS help reduce friction, they are also used in a variety of other industries, including aerospace, automotive, building and construction, and electronics.

Why are PFAS a possible health concern?

According to the U.S. Environmental Protection Agency (EPA), PFAS are considered emerging contaminants. An "emerging contaminant" is a chemical or material that is characterized by a perceived, potential, or real threat to human health or the environment or by a lack of published health standards.

PFAS are extremely persistent in the environment and resistant to typical environmental degradation processes. The pathway for dispersion of these chemicals appears to be long-range atmospheric and oceanic currents transport. Several PFAS and their potential precursors are ubiquitous in a variety of environments. Some long-chain PFAS bioaccumulate in animals and can enter the human food chain.

PFOS and PFOA are two of the most studied PFAS. Exposure to PFOA and PFOS is widespread and global. PFOS and PFOA also persist in the human body and are eliminated slowly. Both PFOS and PFOA can be found in the blood, and at much lower levels in urine, breast milk and in umbilical cord blood.

PFOS and PFOA may pose potential adverse effects for human health given their potential toxicity, mobility, and bioaccumulation potential. The likelihood of adverse effects depends on several factors such as amount and concentration of PFAS ingested as well as the time span of exposure.

Routes of Exposure and Health Effects

What are the main sources of exposure to PFAS?

For the general population, ingestion of PFAS is considered the major human exposure pathway. The major types of human exposure sources for PFAS include:

- Drinking contaminated water.
- Ingesting food contaminated with PFAS, such as certain types of fish and shellfish.
- Until recently, eating food packaged in materials containing PFAS (e.g., popcorn bags, fast food containers, and pizza boxes). Using PFAS compounds has been largely phased out of food packaging materials.
- Hand-to-mouth transfer from surfaces treated with PFAS-containing stain protectants, such as carpets, which is thought to be most significant for infants and toddlers.

National Center for Environmental Health
Agency for Toxic Substances and Disease Registry

CDC ATSDR

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Questions?

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