

**PHS PUBLIC ACCESS**

Author manuscript

*JAMA Pediatr.* Author manuscript; available in PMC 2017 January 05.

Published in final edited form as:

*JAMA Pediatr.* 2016 June 01; 170(6): 609–616. doi:10.1001/jamapediatrics.2016.0120.

## Association of Rice and Rice-Product Consumption With Arsenic Exposure Early in Life

**Margaret R. Karagas, PhD, Tracy Punshon, PhD, Vicki Sayarath, MPH, Brian P. Jackson, PhD, Carol L. Folt, PhD, and Kathryn L. Cottingham, PhD**

Children's Environmental Health and Disease Prevention Research Center, Dartmouth College, Hanover, New Hampshire (Karagas, Punshon, Sayarath, Jackson, Folt, Cottingham); Department of Epidemiology, Geisel School of Medicine, Dartmouth College, Lebanon, New Hampshire (Karagas, Sayarath); Department of Biological Sciences, Dartmouth College, Hanover, New Hampshire (Punshon, Folt, Cottingham); Trace Element Analysis Core Laboratory, Department of Earth Sciences, Dartmouth College, Hanover, New Hampshire (Jackson); University of North Carolina at Chapel Hill (Folt)

### Abstract

**IMPORTANCE**—Rice—a typical first food and major ingredient in various infant foods—contains inorganic arsenic (As), but the extent of As exposure from these foods has not been well characterized in early childhood.

**OBJECTIVE**—To determine the types and frequency of rice and rice-containing products consumed by infants in the first year of life and the association with As biomarker concentrations.

**DESIGN, SETTING, AND PARTICIPANTS**—Included were infants from singleton births of pregnant women enrolled in the New Hampshire Birth Cohort Study from 2011 to 2014 whose parents were interviewed during their first year of life. Enrolled women from selected clinics were aged 18 to 45 years, living in the same residence since their last menstrual period, in households

---

**Corresponding Author:** Margaret R. Karagas, PhD, Department of Epidemiology, Geisel School of Medicine, Dartmouth College, 1 Medical Center Dr, 7927 Ruben Bldg, Lebanon, NH 03766 ([margaret.karagas@dartmouth.edu](mailto:margaret.karagas@dartmouth.edu)).

**Author Audio Interview** at [jamapediatrics.com](http://jamapediatrics.com)

**Supplemental content** at [jamapediatrics.com](http://jamapediatrics.com)

**Author Contributions:** Dr Karagas had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

*Study concept and design:* Karagas, Folt, Cottingham.

*Acquisition, analysis, or interpretation of data:* Karagas, Punshon, Sayarath, Jackson, Cottingham.

*Drafting of the manuscript:* Karagas, Punshon, Jackson, Cottingham.

*Critical revision of the manuscript for important intellectual content:* Karagas, Punshon, Sayarath, Folt, Cottingham.

*Statistical analysis:* Karagas, Punshon, Cottingham.

*Obtained funding:* Karagas, Punshon, Folt, Cottingham.

*Administrative, technical, or material support:* All authors.

*Study supervision:* Karagas, Sayarath, Jackson, Cottingham.

**Conflict of Interest Disclosures:** None reported.

**Disclaimer:** The contents of this article are solely the responsibility of the grantee and do not necessarily represent the official views of the Environmental Protection Agency. Further, the Environmental Protection Agency does not endorse the purchase of any commercial products or services mentioned in the publication.

**Additional Contributions:** The authors are indebted to the participants in the New Hampshire Birth Cohort Study, clinical staff, and physicians and study team. We also gratefully acknowledge the assistance of Courtney Carignan, PhD (Harvard T. H. Chan School of Public Health), in the collection of urine samples. Dr Carignan was compensated for her efforts as a postdoctoral fellow.

served by a private water system, and had no plans to move during pregnancy. Data on infants' intake of rice and rice products were collected from interviews with their parents at 4, 8, and 12 months' follow-up and from a 3-day food diary at 12 months from March 2013 to August 2014.

**EXPOSURES**—Infants' intake of rice and rice products.

**MAIN OUTCOMES AND MEASURES**—Total urinary As and the sum of As species measured using inductively coupled mass spectrometry and high-performance liquid chromatography with inductively coupled mass spectrometry. Commonly reported infant rice snacks were tested for As.

**RESULTS**—We obtained dietary data on 759 of 951 infants (79.8% participation rate). Of these, 391 infants (51.7%) were male, and the mean (SD) gestational age was 39.4 (1.7) weeks. An estimated 80% were introduced to rice cereal during their first year. At 12 months, 32.6% of infants (42 of 129) were fed rice snacks. Among infants aged 12 months who did not eat fish or seafood, the geometric mean total urinary As concentrations were higher among those who ate infant rice cereal (9.53 µg/L) or rice snacks (4.97 µg/L) compared with those who did not eat rice or rice products (2.85 µg/L; all  $P < .01$ ). Infant rice snacks contained between 36 and 568 ng/g of As and 5 to 201 ng/g of inorganic As.

**CONCLUSIONS AND RELEVANCE**—Our findings indicate that intake of rice cereal and other rice-containing foods, such as rice snacks, contribute to infants' As exposure and suggest that efforts should be made to reduce As exposure during this critical phase of development.

Arsenic (As) exposure from rice is of particular concern for infants and children.<sup>1–4</sup> Infant rice cereal, a common first food,<sup>5,6</sup> may contain inorganic As concentrations exceeding the recommendation from the Codex Alimentarius Commission of the World Health Organization and the Food and Agriculture Organization of the United Nations of 200 ng/g for polished (white) rice,<sup>4</sup> the new European Union regulations of 100 ng/g for products aimed at infants<sup>7</sup> (eTable 1 in the Supplement), and the proposed US Food and Drug Administration limit.<sup>8</sup> Infants consuming only a few servings of rice cereal or other products (eg, rice snacks) per day may exceed the now-withdrawn provisional weekly tolerable intakes for As set by the Joint Food and Agriculture Organization of the United Nations and the World Health Organization Expert Committee on Food Additives.<sup>9,10</sup>

Intake of rice early in childhood has not been well characterized in the United States, and there are only limited data from other regions of the world.<sup>5,6</sup> Moreover, biomarker concentrations of As among infants consuming rice are virtually unknown. An association between rice consumption and urinary As would be expected based on previous studies,<sup>11–18</sup> including work from our group on rice consumption during pregnancy,<sup>19</sup> on elevated As concentrations in second- and third-stage infant foods,<sup>20</sup> and on toddler formulas sweetened with brown rice syrup.<sup>21</sup> Emerging epidemiologic evidence suggests that As exposure in utero and during early life may be associated with adverse health effects on fetal growth<sup>22,23</sup> and on infant and child immune<sup>24,25</sup> and neurodevelopmental<sup>26</sup> outcomes, even at the relatively low levels of exposure common in the United States. Given the vulnerability of infants and young children to the effects of As exposure,<sup>27</sup> we investigated food-borne sources of As among infants during the first year of life as part of a US pregnancy cohort.

## Methods

### Study Participants

Our study included 951 of 984 infants (96.6%) delivered to mothers enrolled in the New Hampshire Birth Cohort Study from February 2011 to October 2014 who consented for the follow-up component. Pregnant women using a private water system, living at the same residence since their last menstrual period, not planning to move prior to delivery, and delivering a singleton birth were recruited from participating prenatal clinics. Women were asked to complete a self-administered lifestyle and medical history questionnaire that included information about their home water supply (eg, drilled or dug well vs spring) and use of water filters. Participants were asked to provide a home tap water sample, which was analyzed using collision cell inductively coupled plasma mass spectrometry (ICP-MS) as described previously.<sup>19</sup> The Committee for the Protection of Human Subjects at Dartmouth College approved this study, and all participants provided written informed consent at enrollment in accordance with guidelines from the committee and were compensated for their participation.

### Follow-up Interviews to Ascertain Diet in All Enrolled Infants

Infants were followed up through a structured telephone interview every 4 months (ie, at 4, 8, and 12 months), which included questions about general dietary patterns (breast and formula feeding), the timing of introduction of solid foods (including rice cereal), and changes in water supply. At 12 months, the interviewer asked about dietary patterns during the past week, including whether the infant had consumed rice cereal, white or brown rice, or foods either made with rice (eg, rice-based snacks such as rice cakes or puffs or dried breakfast cereals containing rice) or sweetened with brown rice syrup (eg, certain brands of cereal bars).

### Urine and Food Diary Collection at 12 Months

In March 2013, we began collecting urine samples along with a 3-day food diary from the parents of infants who received pediatric care at the 2 major clinics involved in our study. Parents were asked to record the time of feedings along with the type and amount of all foods and beverages consumed for 3 days, ending at the time the urine sample was obtained. Urine was collected following a protocol adapted from Fångström et al,<sup>28</sup> with diapers and cotton pads tested for As content,<sup>29</sup> analyzed for specific gravity using a handheld refractometer with automatic temperature compensation (PAL-10S; ATAGO Co Ltd), processed, and frozen at  $-80^{\circ}\text{C}$  within 24 hours.

Total urinary As was measured by collision cell ICP-MS using germanium as an internal standard.<sup>30</sup> Arsenic species were obtained by a high-performance liquid chromatography GP50 pump (Dionex Corp) and a PRP100X column (Hamilton Co) connected to a collision cell ICP-MS.<sup>29,31–33</sup> Approximately 10% of samples were run in duplicate for both analyses. The limit of detection for total urinary As was  $0.05\ \mu\text{g/L}$  and was 0.078, 0.15, 0.174, and 0.15 for  $\text{As}^{\text{III}}$ ,  $\text{As}^{\text{V}}$ , monomethylarsonic acid<sup>V</sup>, and dimethylarsinic acid<sup>V</sup>, respectively, and the coefficient of variation for the sum of the metabolites remained less than 10%. The As speciation standard reference materials were National Institute of

Standards and Technology 2669 (levels 1 and 2) and Institut National de Santé Publique Québec S0905, S0909, S0911, S1002, S1015, and S1017 and included 2 urine samples from the Center for Toxicology of Quebec. Average recoveries were all within 15%.

### Market Basket Study of Infant Rice Snacks

Rice snacks frequently reported in the infant food diaries were purchased from online sources and a local supermarket in Hanover, New Hampshire. Duplicate samples were obtained and analyzed for each product. For products with As concentrations of more than 300 ng/g, a different lot number sample was purchased and tested using ICP-MS for total As and high-performance liquid chromatography with ICP-MS for As species. Quality control included duplicate analyses of all samples and 1 sample spike, National Institute of Standards and Technology standard reference materials (1568b), 2 fortified blanks, and 2 digestion blanks. Recoveries were all within the 95% CIs of the certified value.

### Statistical Analysis

We estimated the timing of the introduction of rice cereal in the first year of life by computing the cumulative proportion of infants who were introduced to rice cereal based on responses to the interval interviews up to 12 months. Using data from the interviews at 12 months, we determined the proportion of infants who had ingested white or brown rice as well as foods made with rice or sweetened with brown rice syrup in the past week.

We calculated the percentage of infants who consumed rice-containing foods during the 2 days prior to the collection of urine samples (based on As excretion rates<sup>34,35</sup>) in the following categories: (1) rice (as the primary ingredient); (2) infant rice cereal (marketed as baby, infant, or toddler/transitional cereals with the primary ingredient as rice); (3) non-infant rice cereal (not specifically marketed to infants); (4) adult food with rice (prepared with rice and not specifically marketed to infants); (5) baby food with rice (marketed as baby foods, toddler foods, or other transitional foods for infants and toddlers prepared with rice as one of the ingredients); and (6) snacks made with rice (marketed as snacks with rice as a listed ingredient).

We evaluated associations between  $\log_{10}$ -transformed urinary As concentrations at 12 months and consumption of rice products using general linear models (GLMs), taking into account urinary dilution by including specific gravity as a covariate in all models.<sup>29</sup> We used  $\log_{10}$  transformations to linearize the association between urinary As concentration and specific gravity and to better meet model assumptions of equal variance and normality. In humans,  $\text{As}^{\text{V}}$  reduces to  $\text{As}^{\text{III}}$  and metabolizes to monomethylarsonic acid and dimethylarsinic acid with S-adenosylmethionine as the methyl donor. Arsenobetaine is an unmetabolized form of As present in seafood and fish. Therefore, models for total urinary As concentrations (TUAs) were restricted to infants who had not consumed seafood or fish during the 3 days prior to the collection of urine samples. We also created a model for the speciated urinary As (SUAs), composed of the sum of the inorganic As species ( $\text{As}^{\text{III}}$  and  $\text{As}^{\text{V}}$ ) and the metabolites of inorganic As (monomethylarsonic acid and dimethylarsinic acid), excluding the 7 participants for whom each of the urinary metabolites of interest were below the method detection limit in at least 1 run. We examined the potential confounding

effects of home tap water As concentration and sex, but because these factors were unrelated to urinary As concentrations, we report only the models including specific gravity.

Using GLMs, we tested a 3-level categorical variable to compare infants who consumed no rice products at all, infants who consumed rice, and infants who consumed foods made with rice. We then performed pairwise comparisons for consumers vs nonconsumers of each of the 6 rice food categories. Infants who consumed multiple kinds of rice products were included with each type of food consumed. Additionally, we used a GLM with all food items (as binary variables) entered into a single model to evaluate the relative contributions of particular food items to  $\log_{10}$ -transformed TUAs and SUAs. Finally, we fit a GLM to  $\log_{10}$ -SUAs and  $\log_{10}$ -TUAs as a function of the total servings of rice products and specific gravity. Statistical significance was assessed at  $P = .05$ .

## Results

As of June 2015, interval telephone interviews regarding infants' diets were completed for 759 of 951 infants (79.8%). More detailed information on diet and total urinary As at 12 months was available for 129 infants approached for the substudy, with data on urinary As species available for 48 infants. The characteristics of the infants were generally similar in the subgroups included in the analyses (Table 1).

### Consumption of Rice and Rice Products During the First Year of Life

Of the 759 infants whose parents consented to a telephone interview during the infants' first year of life, an estimated 80% of infants were introduced to rice cereal in the first year of life, with most (64%) starting at 4 to 6 months (eFigure 1 in the Supplement). At 12 months, 43% reported eating some type of rice product in the past week; 13% ate white rice and 10% ate brown rice at an average of 1 to 2 servings per week. Twenty-four percent of infants consumed foods made with rice or sweetened with rice syrup in the past week (eg, rice-based snack foods, nonbaby cereals, and certain cereal bars) at an average of 5 to 6 servings per week.

Based on information recorded in the food diary 2 days prior to the collection of urine samples, 42 of 129 infants (32.6%) ate rice snacks (most of which were specifically recorded as infant or toddler snacks), 13 (10.1%) ate infant or toddler foods containing rice, and 8 (6.2%) ate adult foods with rice. Ten infants (7.8%) consumed white or brown rice, 8 (6.2%) ate baby rice cereal, and 6 (4.7%) ate nonbaby rice cereal (Figure 1A). Overall, 71 infants (55.0%) consumed some type of rice product in the prior 2 days.

### Association of Urinary Arsenic Concentration With Rice Consumption at 12 Months

The median (range) urinary As concentrations were 4.11  $\mu\text{g/L}$  (0.36–121.42  $\mu\text{g/L}$ ) for TUAs, 0.24  $\mu\text{g/L}$  (below detection limit, 2.90  $\mu\text{g/L}$ ) for inorganic As, 0.92  $\mu\text{g/L}$  (below detection limit, 3.07  $\mu\text{g/L}$ ) for monomethylarsonic acid, 3.00  $\mu\text{g/L}$  (below detection limit, 16.46  $\mu\text{g/L}$ ) for dimethylarsinic acid, and 4.06  $\mu\text{g/L}$  (1.05–19.93  $\mu\text{g/L}$ ) for SUAs (eTable 2 in the Supplement). Based on the 129 urine samples at 12 months, As concentrations were higher among infants who consumed rice or foods mixed with rice compared with infants who ate no rice (Figure 2 and Figure 3). Total urinary As concentrations were twice as high among

infants who consumed white or brown rice (geometric mean [GM], 5.83  $\mu\text{g/L}$ ; 95% CI, 4.23–8.05  $\mu\text{g/L}$ ) compared with those who reported no rice intake (GM, 2.85  $\mu\text{g/L}$ ; 95% CI, 2.42–3.34  $\mu\text{g/L}$ ) and were intermediately elevated among infants who consumed foods mixed with rice (GM, 4.13  $\mu\text{g/L}$ ; 95% CI, 3.29–5.18  $\mu\text{g/L}$ ). These differences were statistically significant (GLM adjusted for specific gravity comparing nonrice eaters with rice eaters,  $P = .002$ ; with mixed rice eaters,  $P = .02$ ).

The highest urinary As concentrations were observed among infants who consumed baby rice cereal (GM, 9.53  $\mu\text{g/L}$ ; 95% CI, 4.12–21.98  $\mu\text{g/L}$ ;  $P = .005$ ) (Figure 1B). Of foods mixed with rice, urinary As concentrations were nearly double for those who consumed rice snacks (GM, 4.97  $\mu\text{g/L}$ ; 95% CI, 3.77–8.76  $\mu\text{g/L}$ ) compared with infants who did not consume rice ( $P < .001$ ). These 2 rice products were related to statistically significant increases in both TUAs (eTable 3 in the Supplement) and SUAs (eTable 4 in the Supplement) in models containing all 6 types of rice products. Based on the difference in the model  $R^2$  for the full model containing rice products and specific gravity vs a reduced model that contained only specific gravity, intake of rice and rice products explained 10% of the variability in  $\log_{10}$ -TUAs among non-seafood or fish consumers and 21% in  $\log_{10}$ -SUAs. Further, both  $\log_{10}$ -TUAs ( $P < .001$ ) (data not shown) and  $\log_{10}$ -SUAs ( $P = .009$ ; eFigure 2 in the Supplement) were positively associated with the number of rice or rice-product servings in GLMs with specific gravity.

### Arsenic Concentrations of Infant Snacks

Total As concentrations ranged from 36.5 to 568 ng/g in the 9 different rice-based infant snack foods reported as being consumed by infants in our study, with roughly an equal distribution between inorganic and methylated As species (Table 2). Arsenic content varied between different flavors of the same variety and brand of rice snack, with notably higher As concentrations in the strawberry-flavored puffed rice snacks, which contained 40% inorganic As (brown and white rice flour were the first 2 listed ingredients).

### Discussion

Most infants in our study were exposed to rice and rice products during the first year of life. Rice cereal was introduced to most infants during weaning, and over half were reportedly consuming at least 1 rice product at 12 months. Infants who consumed rice and rice products, including infant rice cereal, had higher urinary As concentrations than those who did not consume any type of rice, with a trend of increasing urinary As concentrations with increasing number of servings of rice and rice products. Moreover, rice snacks marketed to infants and toddlers were reported for nearly one-third of our sample, and some of these products contained inorganic As above the 100 ng/g European Union standard for inorganic As in products geared toward infants.

Arsenic exposure through food, particularly rice and rice products, is a growing concern.<sup>2,3,9,11,20,21,36,37</sup> Rice (*Oryza sativa* L.) appears to accumulate As more than other cereal crops,<sup>38,39</sup> especially when grown in flooded paddies.<sup>40</sup> Both the total concentration of As and the proportion of inorganic As present in commercial rice vary widely owing to differences in rice cultivars and geographical locations.<sup>41–43</sup> Rice from the United States has

higher total As concentrations reported than rice from other countries,<sup>44,45</sup> but no statutory limits for As exist for rice sold in the United States.

Limited information is available on the timing of the introduction of rice cereal or the prevalence of rice-product consumption among US infants. In a cohort study<sup>46</sup> of 1560 children from Denver, Colorado, 87% of infants at high risk for celiac disease (more likely on gluten-free diets) were introduced to rice by 6 months. In a study<sup>6</sup> from Cork, Ireland, baby rice was the first food for 69% of infants. Among infants (6 to 11 months) from the 2002 US Feeding Infants and Toddlers Study,<sup>5</sup> about 16% of Hispanic and 5% of non-Hispanic infants consumed rice. Rice intake was far more prevalent in our study, perhaps reflecting temporal differences or incomplete ascertainment of rice-containing products in the 2002 survey.

Urinary As concentrations in our infants were an order of magnitude lower than the median 35 µg/L of As in a Bangladeshi population exposed to high drinking water As levels (median, 80 µg/L).<sup>28,47</sup> This was expected given the high rate of breastfeeding in our populations<sup>29</sup> and the lower proportion of households with tap water As concentrations above the US Environmental Protection Agency standard of 10 µg/L (12.5% in our study). Thus, our study represents a population for which diet is likely the main source of As exposure. While we are unaware of any prior studies relating As biomarker concentrations to rice intake among infants, associations have been observed in pregnant women in our cohort,<sup>19</sup> children in the National Health and Nutrition Examination Survey,<sup>16,18</sup> and multiple studies of adults.<sup>11–15</sup>

Arsenic concentrations in rice-based snacks we tested were in the range reported in previous studies (eTable 1 in the Supplement), with the exception of 1 product having a total As concentration averaging close to 600 ng/g. Two puffed grain rice snacks were tested by the US Food and Drug Administration; the banana flavor had a total As concentration of 109 ng/g (46 ng/g inorganic), and the blueberry flavor was below the limit of quantitation of 3 ng/g.<sup>45</sup> In the study by Signes-Pastor et al,<sup>10</sup> As concentrations in 97 rice crackers from 15 different brands ranged from 19 to 246 ng/g, with inorganic As ranging from 19 to 212 ng/g.

There are limitations to our study. Our population from northern New England using private, unregulated water systems may not represent the diets of populations elsewhere. This may affect the generalizability of our results, but we would not expect comparisons of rice intake and urinary As to have been biased. The lack of association with certain rice products could have been because of limited statistical power or variability of As content within products. Moreover, other dietary sources of As, such as apple juice, may be further contributing to urinary As concentrations. In our study, dietary intake relied on self-report, but this approach tends to produce an accurate representation of actual diet.<sup>48</sup>

## Conclusions

Arsenic found in rice and rice products can be either in the inorganic or organic form, whereas virtually all drinking water As is inorganic. The toxic effects of inorganic As are clear, and laboratory evidence suggest that organic forms also may pose a health risk,<sup>32</sup>

although further data are needed. The European Food Safety Authority Panel<sup>3</sup> estimated that children younger than 3 years consume 2 to 3 times the amount of inorganic As from food than adults per kilograms of body weight. In addition to being more highly exposed to As, children appear to be far more sensitive to the potential carcinogenic effects of As<sup>49,50</sup> and have a heightened risk for adverse growth, adverse immune response, and adverse neurodevelopmental outcomes,<sup>25,51–53</sup> even at relatively low levels of exposure.<sup>24,54</sup> Our results indicate that consumption of rice and rice products increases infants' exposure to As and that regulation could reduce As exposure during this critical phase of development.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgments

**Funding/Support:** This work was supported by grant P01ES022832 from the National Institute of Environmental Health Sciences and grant RD83544201 from the US Environmental Protection Agency.

**Role of the Funder/Sponsor:** The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript; nor the decision to submit the manuscript for publication.

## References

1. Carignan CC, Punshon T, Karagas MR, Cottingham KL. Potential exposure to arsenic from infant rice cereal [published online [published online March 4, 2016]. *Ann Glob Health*.
2. Lai PY, Cottingham KL, Steinmaus C, Karagas MR, Miller MD. Arsenic and rice: translating research to address health care providers' needs. *J Pediatr*. 2015; 167(4):797–803. [PubMed: 26253210]
3. European Food Safety Authority Panel on Contaminants in the Food Chain. Scientific opinion on arsenic in food: EFSA panel on contaminants in the food chain (CONTAM). *Eur Food Safe Auth J*. 2009; 7(10):1–199. DOI: 10.2903/j.efsa.2009.1351
4. Joint Food and Agriculture Organization of the United Nations/World Health Organization Codex Alimentarius Commission. Report of the eighth session of the codex committee on contaminants in foods. [ftp://ftp.fao.org/codex/Reports/Reports\\_2014/REP14\\_CFe.pdf](ftp://ftp.fao.org/codex/Reports/Reports_2014/REP14_CFe.pdf). Accessed September 4, 2015
5. Mennella JA, Ziegler P, Briefel R, Novak T. Feeding Infants and Toddlers Study: the types of foods fed to Hispanic infants and toddlers. *J Am Diet Assoc*. 2006; 106(1(suppl 1)):S96–S106. [PubMed: 16376634]
6. O'Donovan SM, Murray DM, Hourihane JO, Kenny LC, Irvine AD, Kiely M. Adherence with early infant feeding and complementary feeding guidelines in the Cork BASELINE Birth Cohort Study. *Public Health Nutr*. 2015; 18(15):2864–2873. [PubMed: 25690944]
7. European Commission. Commission regulation (EU) 2015/1006 of 25 June 2015 amending Regulation (EC) 1881/2006 as regards maximum levels of inorganic arsenic in foodstuffs. <http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32015R1006&from=EN>. Accessed September 4, 2015
8. FDA Proposes limit for inorganic arsenic in infant rice cereal [news release]. Silver Spring, MD: Food and Drug Administration; Apr 1. 2016 <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm493740.htm>. Accessed April 1, 2016
9. Meharg AA, Sun G, Williams PN, et al. Inorganic arsenic levels in baby rice are of concern. *Environ Pollut*. 2008; 152(3):746–749. [PubMed: 18339463]
10. Signes-Pastor AJ, Carey M, Meharg AA. Inorganic arsenic in rice-based products for infants and young children. *Food Chem*. 2016; 191:128–134. [PubMed: 26258711]



11. Meharg AA, Williams PN, Deacon CM, et al. Urinary excretion of arsenic following rice consumption. *Environ Pollut*. 2014; 194:181–187. [PubMed: 25145278]
12. Cascio C, Raab A, Jenkins RO, Feldmann J, Meharg AA, Haris PI. The impact of a rice based diet on urinary arsenic. *J Environ Monit*. 2011; 13(2):257–265. [PubMed: 21180691]
13. Wei Y, Zhu J, Nguyen A. Rice consumption and urinary concentrations of arsenic in US adults. *Int J Environ Health Res*. 2014; 24(5):459–470. [PubMed: 24236891]
14. Wu H, Grandjean P, Hu FB, Sun Q. Consumption of white rice and brown rice and urinary inorganic arsenic concentration. *Epidemiology*. 2015; 26(6):e65–e67. [PubMed: 26302090]
15. He Y, Zheng Y. Assessment of in vivo bioaccessibility of arsenic in dietary rice by a mass balance approach. *Sci Total Environ*. 2010; 408(6):1430–1436. [PubMed: 20071009]
16. Davis MA, Mackenzie TA, Cottingham KL, Gilbert-Diamond D, Punshon T, Karagas MR. Rice consumption and urinary arsenic concentrations in US children. *Environ Health Perspect*. 2012; 120(10):1418–1424. [PubMed: 23008276]
17. Davis MA, Gilbert-Diamond D, Karagas MR, et al. A dietary-wide association study (DWAS) of environmental metal exposure in US children and adults. *PLoS One*. 2014; 9(9):e104768. [PubMed: 25198543]
18. deCastro BR, Caldwell KL, Jones RL, et al. Dietary sources of methylated arsenic species in urine of the United States population, NHANES 2003–2010. *PLoS One*. 2014; 9(9):e108098. [PubMed: 25251890]
19. Gilbert-Diamond D, Cottingham KL, Gruber JF, et al. Rice consumption contributes to arsenic exposure in US women. *Proc Natl Acad Sci U S A*. 2011; 108(51):20656–20660. [PubMed: 22143778]
20. Jackson BP, Taylor VF, Punshon T, Cottingham KL. Arsenic concentration and speciation in infant formulas and first foods. *Pure Appl Chem*. 2012; 84(2):215–223. [PubMed: 22701232]
21. Jackson BP, Taylor VF, Karagas MR, Punshon T, Cottingham KL. Arsenic, organic foods, and brown rice syrup. *Environ Health Perspect*. 2012; 120(5):623–626. [PubMed: 22336149]
22. Davis MA, Higgins J, Li Z, et al. Preliminary analysis of in utero low-level arsenic exposure and fetal growth using biometric measurements extracted from fetal ultrasound reports. *Environ Health*. 2015; 14:12. [PubMed: 25971349]
23. Fei DL, Koestler DC, Li Z, et al. Association between in utero arsenic exposure, placental gene expression, and infant birth weight: a US birth cohort study. *Environ Health*. 2013; 12:58. [PubMed: 23866971]
24. Farzan SF, Li Z, Korrick SA, et al. Infant infections and respiratory symptoms in relation to in utero arsenic exposure in a US cohort [published online September 11, 2015]. *Environ Health Perspect*.
25. Nadeau KC, Li Z, Farzan S, et al. In utero arsenic exposure and fetal immune repertoire in a US pregnancy cohort. *Clin Immunol*. 2014; 155(2):188–197. [PubMed: 25229165]
26. Wasserman GA, Liu X, Loiacono NJ, et al. A cross-sectional study of well water arsenic and child IQ in Maine schoolchildren. *Environ Health*. 2014; 13(1):23. [PubMed: 24684736]
27. Farzan SF, Karagas MR, Chen Y. In utero and early life arsenic exposure in relation to long-term health and disease. *Toxicol Appl Pharmacol*. 2013; 272(2):384–390. [PubMed: 23859881]
28. Fångström B, Moore S, Nermell B, et al. Breast-feeding protects against arsenic exposure in Bangladeshi infants. *Environ Health Perspect*. 2008; 116(7):963–969. [PubMed: 18629322]
29. Carignan CC, Cottingham KL, Jackson BP, et al. Estimated exposure to arsenic in breastfed and formula-fed infants in a United States cohort. *Environ Health Perspect*. 2015; 123(5):500–506. [PubMed: 25707031]
30. McCurdy E, Woods G. The application of collision/reaction cell inductively coupled plasma mass spectrometry to multi-element analysis in variable sample matrices, using He as a non-reactive cell gas. *J Anal At Spectrom*. 2004; 19(5):607–615. DOI: 10.1039/B312250F
31. Larsen EH, Pritzl G, Hansen SH. Speciation of eight arsenic compounds in human urine by high-performance liquid-chromatography with inductively-coupled plasma-mass spectrometric detection using antimonate for internal chromatographic standardization. *J Anal At Spectrom*. 1993; 8:557–563. DOI: 10.1039/JA9930800557

32. Le XC, Ma M, Cullen WR, Aposhian HV, Lu X, Zheng B. Determination of monomethylarsonous acid, a key arsenic methylation intermediate, in human urine. *Environ Health Perspect.* 2000; 108(11):1015–1018.
33. Wei HY, Brockhoff-Schwegel CA, Creed JT. A comparison of urinary arsenic speciation via direct nebulization and on-line photo-oxidation-hydride generation with IC separation and ICP-MS detection. *J Anal At Spectrom.* 2001; 16:12–19. DOI: 10.1039/B004257I
34. Zheng Y, Wu J, Ng JC, Wang G, Lian W. The absorption and excretion of fluoride and arsenic in humans. *Toxicol Lett.* 2002; 133(1):77–82. [PubMed: 12076512]
35. Francesconi KA, Tanggaar R, McKenzie CJ, Goessler W. Arsenic metabolites in human urine after ingestion of an arsenosugar. *Clin Chem.* 2002; 48(1):92–101. [PubMed: 11751543]
36. Hojsak I, Braegger C, Bronsky J, et al. ESPGHAN Committee on Nutrition. Arsenic in rice: a cause for concern. *J Pediatr Gastroenterol Nutr.* 2015; 60(1):142–145. [PubMed: 25536328]
37. Souza JM, Carneiro MF, Paulelli AC, et al. Arsenic and rice: toxicity, metabolism, and food safety [in Portuguese]. *Quim Nova.* 2015; 38(1):118–127. DOI: 10.5935/0100-4042.20140279
38. Mitani N, Chiba Y, Yamaji N, Ma JF. Identification and characterization of maize and barley Lsi2-like silicon efflux transporters reveals a distinct silicon uptake system from that in rice. *Plant Cell.* 2009; 21(7):2133–2142. [PubMed: 19574435]
39. Williams PN, Villada A, Deacon C, et al. Greatly enhanced arsenic shoot assimilation in rice leads to elevated grain levels compared to wheat and barley. *Environ Sci Technol.* 2007; 41(19):6854–6859. [PubMed: 17969706]
40. Takahashi Y, Minamikawa R, Hattori KH, Kurishima K, Kihou N, Yuita K. Arsenic behavior in paddy fields during the cycle of flooded and non-flooded periods. *Environ Sci Technol.* 2004; 38(4):1038–1044. [PubMed: 14998016]
41. Zhao FJ, Zhu YG, Meharg AA. Methylated arsenic species in rice: geographical variation, origin, and uptake mechanisms. *Environ Sci Technol.* 2013; 47(9):3957–3966. [PubMed: 23521218]
42. Roy P, Orikasa T, Okadome H, Nakamura N, Shiina T. Processing conditions, rice properties, health and environment. *Int J Environ Res Public Health.* 2011; 8(6):1957–1976. [PubMed: 21776212]
43. Rahman MA, Hasegawa H, Rahman MM, Rahman MA, Miah MA. Accumulation of arsenic in tissues of rice plant (*Oryza sativa* L.) and its distribution in fractions of rice grain. *Chemosphere.* 2007; 69(6):942–948. [PubMed: 17599387]
44. Meharg AA, Williams PN, Adomako E, et al. Geographical variation in total and inorganic arsenic content of polished (white) rice. *Environ Sci Technol.* 2009; 43(5):1612–1617. [PubMed: 19350943]
45. US Food and Drug Administration. Analytical results from inorganic arsenic in rice and rice products sampling. <http://www.fda.gov/downloads/Food/FoodborneIllnessContaminants/Metals/UCM352467.pdf>. Accessed September 4, 2015
46. Norris JM, Barriga K, Hoffenberg EJ, et al. Risk of celiac disease autoimmunity and timing of gluten introduction in the diet of infants at increased risk of disease. *JAMA.* 2005; 293(19):2343–2351. [PubMed: 15900004]
47. Hamadani JD, Grantham-McGregor SM, Tofail F, et al. Pre- and postnatal arsenic exposure and child development at 18 months of age: a cohort study in rural Bangladesh. *Int J Epidemiol.* 2010; 39(5):1206–1216. [PubMed: 20085967]
48. Willett W. Commentary: dietary diaries versus food frequency questionnaires: a case of undigestible data. *Int J Epidemiol.* 2001; 30(2):317–319. [PubMed: 11369736]
49. Bailey KA, Smith AH, Tokar EJ, et al. Mechanisms underlying latent disease risk associated with early-life arsenic exposure: current research trends and scientific gaps. *Environ Health Perspect.* 2015; 124(2):170–175. [PubMed: 26115410]
50. Smith AH, Marshall G, Liaw J, Yuan Y, Ferreccio C, Steinmaus C. Mortality in young adults following in utero and childhood exposure to arsenic in drinking water. *Environ Health Perspect.* 2012; 120(11):1527–1531. [PubMed: 22949133]
51. Wasserman GA, Liu X, Parvez F, et al. Water arsenic exposure and intellectual function in 6-year-old children in Arahazar, Bangladesh. *Environ Health Perspect.* 2007; 115(2):285–289. [PubMed: 17384779]

52. Ahmed S, Moore SE, Kippler M, et al. Arsenic exposure and cell-mediated immunity in pre-school children in rural Bangladesh. *Toxicol Sci.* 2014; 141(1):166–175. [PubMed: 24924402]
53. Rodríguez-Barranco M, Lacasaña M, Aguilar-Garduño C, et al. Association of arsenic, cadmium and manganese exposure with neurodevelopment and behavioural disorders in children: a systematic review and meta-analysis. *Sci Total Environ.* 2013; 454–455:562–577.
54. Farzan SF, Korrick S, Li Z, et al. In utero arsenic exposure and infant infection in a United States cohort: a prospective study. *Environ Res.* 2013; 126:24–30. [PubMed: 23769261]

### Key Points

**Question**

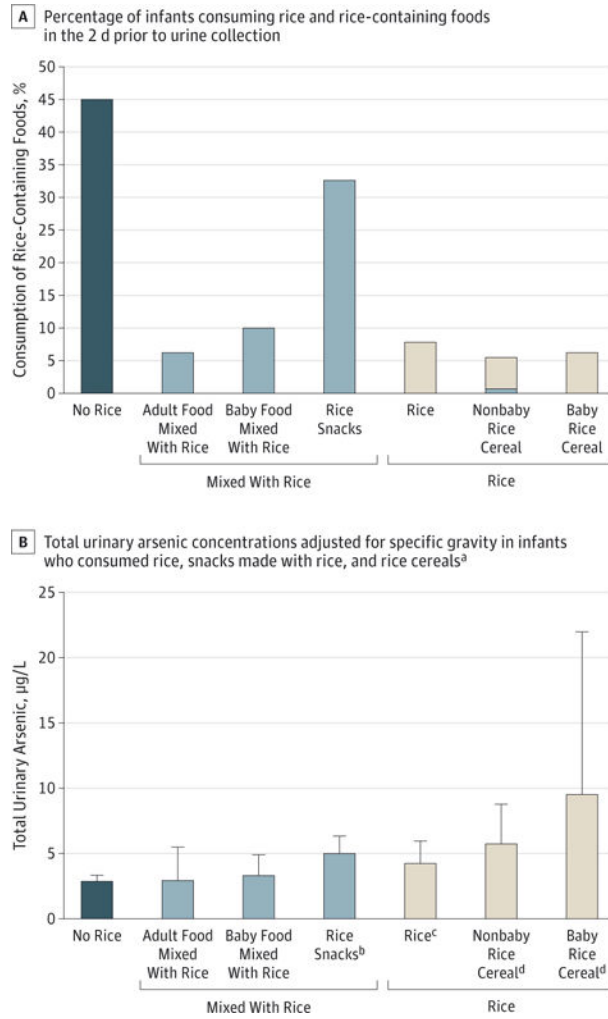
How frequently do infants consume rice and rice-containing products, and what is their exposure to arsenic from these foods?

**Findings**

In this cohort study of 759 infants with dietary data, an estimated 80% were introduced to rice cereal in the first year of life. In a subset of 129 infants studied at 12 months of age, 55% reported consuming rice or rice products, including rice snacks, in the 2 days prior to urine collection, and consumption of these products was associated with urinary arsenic concentrations in infants.

**Meaning**

These findings suggest that infants' consumption of rice and rice-containing foods, typical of their diets, contribute to their arsenic exposure and highlight the need for strategies to reduce exposure during this critical phase of development.



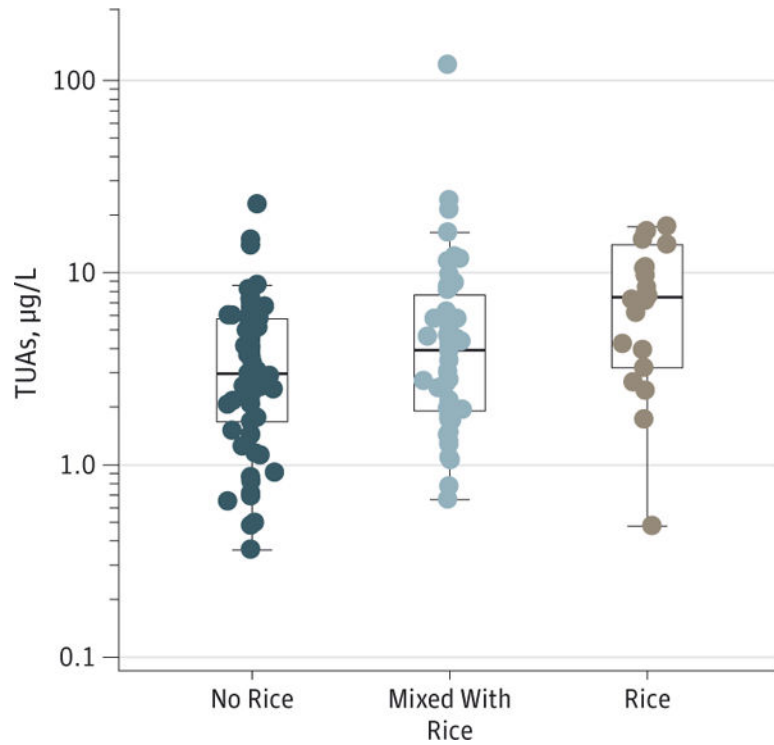
**Figure 1. Prevalence of Rice and Rice-Product Consumption and Association With Urinary Arsenic Concentrations Among 129 Infants at 12 Months**

<sup>a</sup>Error bars indicate the back-transformed confidence intervals.

<sup>b</sup> $P < .001$  for pairwise comparisons of infants who consumed rice with infants who consumed no rice or rice products in general linear models that also included specific gravity.

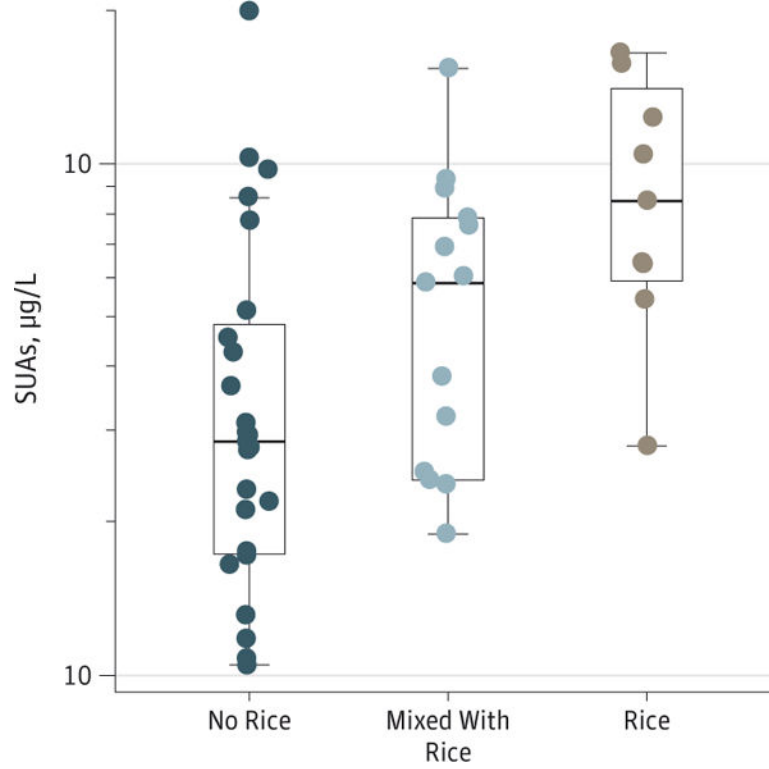
<sup>c</sup> $P < .05$  for pairwise comparisons of infants who consumed rice with infants who consumed no rice or rice products in general linear models that also included specific gravity.

<sup>d</sup> $P < .01$  for pairwise comparisons of infants who consumed rice with infants who consumed no rice or rice products in general linear models that also included specific gravity.



**Figure 2. Log<sub>10</sub>-Transformed Total Urinary Arsenic (TUAs) According to Rice Food Intake Among 129 Infants**

$P < .001$  from a general linear model including specific gravity to account for urinary dilution and the 3 rice food intake categories ( $F_{2,130} = 9.55$ ). Infants who did not consume rice had lower log<sub>10</sub>-transformed TUAs than infants who consumed either foods mixed with rice (Tukey honestly significant difference test,  $P = .02$ ) or pure rice (Tukey honestly significant difference test,  $P < .001$ ). There was no difference between infants who consumed foods mixed with rice or pure rice (Tukey honestly significant difference test,  $P = .14$ ).



**Figure 3. Log<sub>10</sub>-Transformed Summed Speciated Urinary Arsenic (SUAs) According to Rice Food Intake Among 48 Infants**

$P < .001$  from a general linear model including specific gravity to account for urinary dilution and the 3 rice food intake categories ( $F_{2,45} = 9.02$ ). Infants who did not consume rice had lower log<sub>10</sub>-transformed SUAs than infants who consumed either foods mixed with rice (Tukey honestly significant difference test,  $P = .04$ ) or pure rice (Tukey honestly significant difference test,  $P < .001$ ). There was no difference between infants who consumed foods mixed with rice or pure rice (Tukey honestly significant difference test,  $P = .20$ ).

**Table 1**

Selected Characteristics of Study Mothers and Infants From the New Hampshire Birth Cohort Study

Characteristic	No. (%) of Infants		
	With Interval Dietary Data (n = 759)	With 12-mo Diaries and TUAs (n = 129)	With 12-mo Diaries and SUAs (n = 48)
Maternal age at enrollment, y			
<20	9 (1.2)	0	0
20–29	294 (38.7)	49 (38.0)	19 (39.6)
30–35	270 (35.6)	54 (41.9)	19 (39.6)
>35	186 (24.5)	26 (20.2)	10 (20.8)
Maternal education			
<11th grade	7/702 (1.0)	1/126 (0.8)	1 (2.1)
High school graduate or GED	68/702 (9.7)	4/126 (3.2)	2 (4.2)
Junior college or some college	131/702 (18.7)	27/126 (21.4)	11 (22.9)
College graduate	280/702 (39.9)	42/126 (33.3)	16 (33.3)
Postgraduate schooling	216/702 (30.8)	52/126 (41.3)	18 (37.5)
Maternal relationship status			
Single	73/702 (10.4)	7/126 (5.6)	4 (8.3)
Married	605/702 (86.2)	117/126 (92.9)	43 (89.6)
Separated or divorced	24/702 (3.4)	2/126 (1.6)	1 (2.1)
Mother smoked during pregnancy			
Yes	46/725 (6.3)	4 (3.1)	2/44 (4.2)
No	679/725 (93.7)	125 (96.9)	42/44 (95.8)
Infant sex			
Male	391/756 (51.7)	72 (55.8)	26/38 (54.2)
Female	365/756 (48.3)	57 (44.2)	12/38 (45.8)
Infant race			
White	752/756 (99.5)	129 (100)	48 (100)
Other	4/756 (0.5)	0	0
Gestational age, mean (SD), wk	39.4 (1.7)	39.4 (1.5)	39.7 (1.4)
Tap water arsenic, µg/L			
<1	514 (67.7)	83 (64.3)	30 (62.5)
1–10	188 (24.8)	37 (28.7)	12 (25.0)
>10	57 (7.5)	9 (7.0)	6 (12.5)

Abbreviations: GED, General Education Development; SUAs, speciated urinary arsenic concentration (the sum of inorganic arsenic, monomethylarsonic acid, and dimethylarsinic acid concentrations); TUAs, total urinary arsenic concentration.



**Table 2**  
Concentration of Arsenic and Its Constituent Species Measured in Infant Snacks (ng/g)

Description	Arsenic Concentration, ng/g						% iAs
	Total, Mean (SD) <sup>a</sup>	iAs	As <sup>III</sup>	As <sup>V</sup>	DMA	MMA	
Cereal snack							
Vanilla	42.4 (3.1)	17.8	17.8	0.0	12.0	0.0	39.8
Puffed grain snack							
Green vegetable	36.5 (2.3)	4.6	4.6	0.0	16.3	0.0	12.2
Banana	75.8 (5.8)	39.7	39.7	0.0	12.6	0.0	49.7
Strawberry	568.1 (69.4) <sup>b</sup>	201.0	149.5	51.5	297.8	8.6	39.5
Carrot, blueberry	309.4 (8.0)	140.9	125.0	15.8	158.0	7.4	46.4
Puffed whole grain snack							
Blueberry	86.1 (3.5) <sup>c</sup>	35.7	35.7	0.0	31.2	0.0	38.0
Rice biscuits							
Apple	117.7 (10.8)	57.2	57.2	0.0	47.6	0.0	52.0
Banana	237.0 (1.4)	60.5	60.5	0.0	48.6	0.0	50.7
Rice rusks							
Original	114.2 (8.4)	42.9	42.9	0.0	63.2	0.0	35.7

Abbreviations: As<sup>III</sup>, arsenite; As<sup>V</sup>, arsenate; DMA, dimethylarsinic acid; iAs, inorganic arsenic; MMA, monomethylarsonic acid.

<sup>a</sup>The total arsenic concentration (the sum of methylated and unmethylated arsenic, excluding arsenobetaine) represents the mean (SD) of duplicate samples from the same lot unless indicated otherwise.

<sup>b</sup>Five individual samples from 2 different lots.

<sup>c</sup>Twelve individual samples from the same lot.