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

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Arsenic is a naturally occurring element and anthropogenic contaminant present in 2 general forms: inorganic and organic. Inorganic arsenic is considered highly toxic to humans.[1] The International Agency for Research on Cancer, Agency for Toxic Substances and Disease Registry, and the US Environmental Protection Agency (EPA) all classify inorganic arsenic as a human carcinogen.[2–4] The health effects of organic forms are not fully understood; however, some of the organic forms also may have toxic and potentially carcinogenic properties.[5]

Children can be exposed to arsenic in multiple ways.[1,3] An important source of chronic exposure to inorganic arsenic worldwide is contaminated drinking water. However, because municipal water systems in the US are regulated to meet federal standards, the primary exposure to arsenic for most people in the US is food.[3] One food known to be particularly high in arsenic is rice, a staple for much of the world's population.[6] Rice grown throughout the world contains arsenic, particularly US-grown rice.[7] Though the amount and forms of arsenic found in different rice cultivars vary, the average levels of inorganic arsenic detected in rice are high enough to raise questions about potential health impacts, including for children.[8–11]

Dietary exposure to arsenic is of particular concern for children for several reasons.[5,12] First, exposure to arsenic and other chemicals during critical windows of vulnerability in early

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childhood may result in greater health risks.[12,13] Second, children typically have greater exposure to contaminants per unit body weight than adults[14] in part because of their greater consumption rates and high caloric needs.[15,16] Finally, children may also be more exposed to contaminants unique to certain foods because of their selective eating patterns and limited dietary choices.[16] For example, rice is used in many first foods[15] and is a key component of numerous processed foods marketed specifically to children.[17] Thus, it is important for clinicians to become familiar with childhood arsenic exposure, potential health effects, and strategies to reduce exposure.

Given the concern about children's consumption of arsenic in rice, the US Food and Drug Administration (FDA) has published brief statements on this topic to encourage families to eat a "well-balanced diet,"[18] and the American Academy of Pediatrics (AAP) suggests that cereals from other grains, finely chopped meats, and vegetable purees are equally acceptable as rice cereal for introduction as first foods,[19] and to consider the use of alternatives, like oats and cornstarch, instead of rice, to thicken first foods.[20] Both organizations, however, have not offered more specific guidance on this issue to the public. This Commentary aims to provide key information for health care providers faced with providing guidance on arsenic exposure from rice consumption for the children before more definitive guidance is issued.

Health Effects Associated with Arsenic Exposure

Health studies of ingested arsenic exposure are limited primarily to exposure from water. Worldwide, over 100 million people are exposed via contaminated drinking water,[7,21] including more than 2 million Americans drinking water from private wells containing arsenic at concentrations above the current World Health Organization and US EPA maximum contaminant level (MCL) of 10 μg As/L.[22,23] Nearly all of the arsenic in groundwater is in inorganic form, known to be toxic.[24] Numerous studies have linked chronic exposure to high levels of arsenic to adverse health effects in multiple organ systems including keratosis; skin, bladder and lung cancers; impaired intellectual function; bronchiectasis; coronary heart disease; and diabetes.[2,3,22,24] According to the National Research Council, the current US EPA drinking water standard of 10 μg/L may be associated with an estimated lifetime excess cancer risk as high as 1 case in 300 people,[24] where a lifetime is considered to be 70 years of exposure. This is 3000 times higher than a commonly accepted cancer risk for an environmental carcinogen of 1 case in 1 000 000 people.

Effects of prenatal and early childhood exposure to high levels of arsenic can be substantial.[25,26] Arsenic readily passes through the placenta,[1,27] and epidemiologic studies in Bangladesh, Chile, and Taiwan have linked in utero exposure to low birth weight,[28] spontaneous abortions, infant mortality,[29–32] and increased risk of lung cancer later in life.[33] Moreover, emerging evidence links maternal exposure to low doses of arsenic in drinking water (~5–10 μg/L) during pregnancy to increased infections during infancy.[34] In contrast, there appears to be limited transfer of arsenic into breast milk in both highly exposed populations[27,35,36] and less exposed populations,[37,38] suggesting that breastfeeding may reduce exposure. Exposure may occur in formula-fed babies through both the formula powder and drinking water.[15,37]

Developing fetuses and children have both enhanced vulnerability and a longer post-exposure lifespan than adults. Effects with long latency periods, such as carcinogenic action, have a greater opportunity to manifest after early life exposure.[16,34] Enhanced vulnerability was identified in research of heavily exposed populations in northern Chile that indicates in utero or early life exposures to ingested arsenic are associated with high mortality rates of bronchiectasis, acute myocardial infarction, and bladder, laryngeal, and lung cancers.[39] Recent data also suggest that in utero or early life exposure is associated with decreased lung function as adults[40] and excess relative risks of lung cancer and bladder cancer, which are 2 to 4 times higher than those who were exposed later in life.[33] Early life exposure has also been associated with neurocognitive and motor impairment,[41–44] as well as decreased IQ.[45]

High Arsenic Concentrations in Rice

Literature regarding the presence of arsenic in rice prompted the US FDA to extensively test different brands of rice grains and rice products sold in the US for inorganic arsenic.[46] Based on data published in 2013, all of the 1343 samples contained inorganic arsenic. Though there is a variable amount of arsenic in the products sampled, nearly one-third (30%) contained high levels of inorganic arsenic (>4 μg per serving), which at a consumption rate of 2.5 servings a day could pose an estimated lifetime excess cancer risk at or above 1 case in 300 people, by comparison with the current water MCL. One of the hot rice bran cereals sampled, though an outlier, contained as much as 30 μg of inorganic arsenic per serving.[46] Moreover, many of the products containing high levels of arsenic may be consumed by children, including rice cakes and bakery mixes/pudding.[46]

Rice generally contains more arsenic than other grains because of its anaerobic growing environment and unique physiology. In flooded rice paddies, arsenic is brought into the plant by its silicon transporters, and then used in place of silicon to strengthen the plant stem and husks, including the part of the plant we eat.[7] There is wide variation in total and inorganic arsenic concentrations across different types of rice and growing locations. Limited sampling indicates that in general, rice grown in the South Central US (Arkansas, Missouri, Louisiana, and Texas) contains more arsenic than rice grown in California.[7,47] This may in part be a result of the historical application of arsenic-containing pesticides from the legacy of cotton production in the region, which has since been converted to rice production.[7,47] In comparing across types and locations, inorganic arsenic concentrations appear to be lowest in sushi rice from the US and Basmati rice from California, India, or Pakistan.[48] Within any one type of rice, brown rice contains more arsenic than white rice because arsenic accumulates in the bran, which is the hard outer layer of the grain seen in brown rice.[7,8] Removal of this layer produces white rice, thereby eliminating a portion of the arsenic. However, the bran also contains nutritious fiber and vitamins,[7] so even though brown rice on average contains more inorganic arsenic, it also provides more nutrition.

Rice is a Major Contributor to Dietary Arsenic Exposure

Studies conducted in the US have shown a positive relationship between rice consumption and urinary arsenic excretion, which is directly related to overall arsenic exposure.[49] Cleland et al found a statistically significant association between rice consumption and urinary arsenic excretion in 67 women of childbearing age of Korean descent from Washington State.[50] Rice was a major source of inorganic arsenic exposure for this population, with an estimated average intake of 16.3 μg of inorganic arsenic from rice per day,[50] comparable with drinking 1.6 L of water at the current US EPA MCL. Another study analyzed 229 pregnant women in New Hampshire who drank private, unregulated well water and found an association between rice consumption and urinary arsenic excretion after correcting for water exposure.[51] Each 1 g increase in rice intake was associated with a 1% increase in urinary total arsenic, such that eating 0.56 cups of cooked rice was considered comparable with drinking 1 L/d of water at the current US EPA MCL.[51]

Dietary Exposure May Be Greater in Infants and Children

The European Food Safety Authority has reported that dietary exposure to inorganic arsenic for children under 3 years old is about 3 times higher than that of adults based on kilogram body weight,[5,12] due in part to the types of foods infants and young children consume. Elevated levels of inorganic arsenic have been found in foods commonly eaten by infants and toddlers, including rice cereals (a common first food), pureed foods, and products sweetened with brown rice syrup.[13,15,17,52,53] Based on measurements of arsenic concentrations by the US FDA, exposure to inorganic arsenic via just one 17-g serving of infant rice cereal per day is estimated to be 0.22–0.60 $\mu g\ kg^{-1}\ d^{-1}$ in 6 to 12-month-old infants (Carignan et al, unpublished data)—an intake well above the 0.17 $\mu g\ kg^{-1}\ d^{-1}$ calculated by Meharg et al[13] to be equivalent in dose to the water MCL threshold established by the US EPA. During the toddler years, lactose-intolerant children may be offered rice milk, which has an average inorganic arsenic concentration of 11.7 μg/L,[12] higher than the water standard.[54] For this reason, the United Kingdom Food Standards Agency recommends that children under 4.5 years of age not use rice milk as a milk substitute.[54] Thus, infants or toddlers consuming rice-containing products may regularly be exposed to unacceptably high levels of arsenic.

Of American children between 1 and 6 years old who have the highest dietary exposure to arsenic (ie, 95th percentile), rice and rice products contribute about 50% of their exposure.[53] Twenty percent of the 2323 children between ages 6 and 17 years sampled in the National Health and Nutrition Examination Survey between 2003 and 2008 reported eating the equivalent of at least one-quarter cup of cooked rice per day.[56] Mean urinary arsenic concentrations (8.9 μg/L) were higher in these “rice eaters” compared with “non-rice eaters” (5.5 μg/L).[56] We further analyzed National Health and Nutrition Examination Survey data from 2003–2008 using the methods described by Davis et al[56] and found a positive relationship between rice consumption and urinary arsenic excretion in children between 6 and 17 years old (Figure 1). The top 1% of rice consumers ate at least 1.75 cups of cooked rice per day and had a median urinary arsenic concentration of 15.0 μg/L, nearly 3 times that of non-rice eating children. Moreover, children who ate a lot of rice – and had higher urinary arsenic concentrations – tended to come from one particular racial group, "Other", which consisted mostly of those of Asian descent (Figure 2). In the analysis used to develop Figures 1 and 2, the rice servings consumed by each NHANES subject were based on food products and intake levels listed in the subjects' 24-hour dietary recalls. Food products containing rice were identified using the US EPA's Dietary Exposure Evaluation Model-Food Commodity Intake Database[55] and converted to servings per day using the methods described by Davis et al.[56] Urinary inorganic arsenic concentration is the sum of inorganic arsenic and its major metabolites, monomethyl- and dimethyl arsenic. Each quarter cup serving of cooked rice is equivalent to 16.5 g of cooked rice.

In older children, sources of arsenic include cereal bars, energy bars, and energy shot blocks that contain brown rice syrup, often marketed as "organic" or healthy.[17] As 1 cereal bar could contain as much as 3.6 *μ*g inorganic arsenic per bar,[17] eating 3 bars a day could pose a very high cancer risk.

Testing Children for Exposure

Although measurements of urinary arsenic concentrations are valuable in research, they have limited value in the clinical setting of evaluating dietary exposure and may not alter management. Part of the challenge is that quantifying overall arsenic exposure from food is difficult because of the variability in day-to-day exposure rates: not only do people's diets vary, but arsenic concentrations in food and the speciation of arsenic into inorganic vs organic components are both highly variable. Thus, a single high arsenic measurement does not explain the source of exposure and a low arsenic concentration cannot rule out significant exposure. Testing is therefore not generally indicated in asymptomatic patients, as there is no evidence-based value for intervention. The clinician could avoid an expense and legitimately counsel patients at risk of high dietary arsenic exposure about reducing exposure based on a dietary history focused on rice and rice-based products. In the case when arsenic biomonitoring is indicated (eg, concern about acute toxicity), it is important to avoid seafood for 1 or 2 weeks prior to urine sample collection to eliminate relatively nontoxic organic arsenic from seafood.[49] Though more costly, a urine sample analyzed for organic and inorganic species is the most informative measurement for recent exposure.

Limitations

Clear evidence linking arsenic to cancer and other health effects comes largely from studies involving high concentrations of inorganic arsenic in water—intake levels that are markedly higher than those typically seen for rice consumption. There is emerging evidence on the impact of lower concentrations of arsenic in water and health outcomes.[5,24,57–59] Issues of inadequate sample sizes, and a greater probability that findings are solely due to confounding or bias, are points of criticism for some of the cancer studies involving lower exposure.[60] As yet, there are few studies of rice consumption and health outcomes. In Bangladesh, steamed rice consumption was associated with both urinary arsenic excretion and occurrence of skin lesions, although this study lacked data on arsenic in water used for cooking and other potential dietary sources of arsenic.[61] Risks associated with low to moderate arsenic exposures have often been based on linear extrapolations from the risks seen at very high exposures.[62,63] Although some criticize these extrapolations because they do not consider the possibility that there is an exposure threshold below which arsenic is not harmful, the existence of a threshold has not been observed in epidemiologic studies.

Discussion

At present, there is no consensus recommendation about the consumption of rice products by children and pregnant women in the US. As noted above, the US FDA and the AAP have published brief statements on this topic that emphasize arsenic intake at the levels in rice is not expected to pose any acute or immediate health effects.[18,20,64] However, no conclusions were drawn about long-term health effects, even though potential risks of serious adverse health effects may be inferred from research on prolonged arsenic ingestion of contaminated water.

The FDA and AAP recommend that families “eat a well-balanced diet” and “eat a variety of grains”. If this means limiting rice consumption, this recommendation may not be adopted by frequent or daily rice eaters who eat rice as their staple grain—particularly for a few key sub-populations: (1) those with a medical condition, like celiac disease or severe food allergies that require specialized foods made with rice fillers; (2) those with restricted diets, such as vegan or macrobiotic diets; or (3) those who eat rice as the staple grain as part of their culture, such as Asians and His-panics who may eat rice 3 or more times a day.[8,11,65,66] For millions of people, rice is an integral part of their culture and emblematic in their rituals. For example, the Land Opening Festival in China marks the beginning of the rice season, and the Japanese refer to rice as their “mother” and regard rice farmers as the guardian of their culture and the countryside.[66] Thus, rice has a very special place in many cultures and diminishing its importance would present enormous cultural challenges along with practical barriers to introducing alternatives that ensure adequate nutrition.

Given the levels of potential exposure to arsenic from rice products noted above, various authorities have prioritized different strategies to reduce individual exposure as reflected in the Table.[8,18,20,54] Though the Food and Agriculture Organization of the United Nations adopted its first nonbinding standard for arsenic content in rice in July 2014,[67] there are currently no food standards for arsenic in rice in the US.

Because children who consume rice daily and infants whose first solid food is rice are at particular risk for high arsenic exposure, one could consider counseling patients and families about reading ingredient labels to be familiar with foodstuffs made from rice and reducing rice intake in general. Simple strategies to reduce exposure without undue consequences include reducing the use of rice cereal as a first food or thickener in infancy, limiting rice milk consumption, avoiding products sweetened with brown rice syrup, and diversifying grains. However, as mentioned, the caveat is that rice reduction or grain substitution may not be realistic for all families given cultural, medical, or other preferences. Moreover, given the widespread and diverse use of rice and rice products, caregivers may not even be aware of the presence of rice in the foods their children consume.

The high levels of arsenic in rice and rice products are worrisome and could be associated with adverse chronic health effects. Though the actual risks are still being defined, extrapolation from previous risk assessments of arsenic exposure from water suggests the possibility of long-term health risks, particularly in the developing fetus and child.[62] Though short-term exposures during sensitive developmental periods of vulnerability may present significant risks to the fetus and children, many of the known health risks are based on long-term exposure. Thus, making dietary changes in childhood may reduce risks. Until the FDA and other authoritative sources provide further information, health care providers should consider cautioning families in culturally sensitive ways and counsel on ways to decrease arsenic exposure from rice (Table).

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Glossary

AAP	American Academy of Pediatrics
EPA	Environmental Protection Agency
FDA	Food and Drug Administration
MCL	Maximum contaminant level

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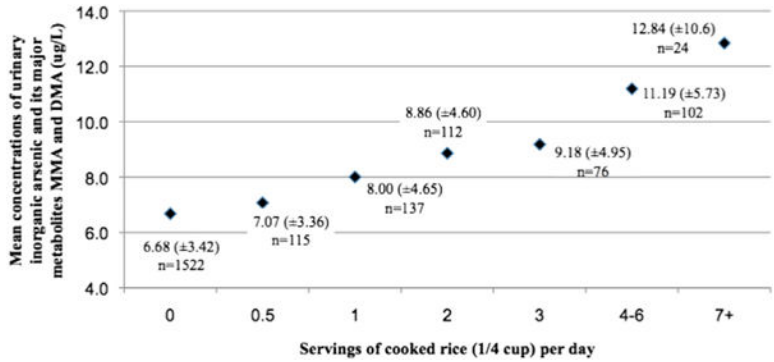

Figure 1.

Mean concentrations of urinary inorganic arsenic and its major metabolites MMA and DMA by categories of rice intake in children ages 6–17, National Health and Nutrition Examination Survey (NHANES) 2003–2008, excluding subjects with recent seafood consumption.

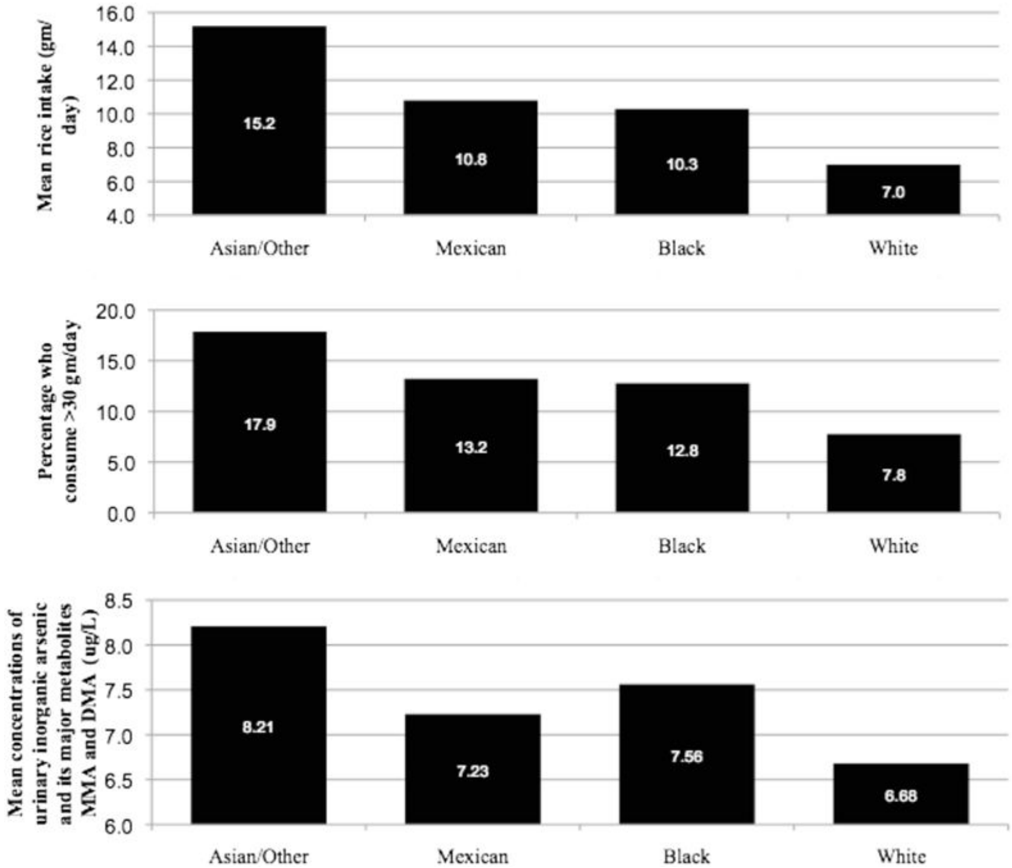

Figure 2.

Mean rice intake levels and mean urinary arsenic concentrations in children ages 6–17 by race, NHANES 2003–2008.

Table

Potential strategies for reducing exposure of arsenic in rice*

1 Diversify the diet

- Eat a well-balanced diet and a variety of grains†,‡,§
- Identify children at risk for high consumption of rice and rice products (eg, gluten-free diets, highly allergic)

2 Consider alternatives to rice for first food

- Start infants on barley, oats, or other grains†,‡
- If rice cereal must be used for infants, limit to 1 serving per day§

3 Adopt strategies that help minimize exposure

- Rinse rice in a colander prior to cooking§
- Cook rice like pasta, with plenty of extra water§
- Choose lower-arsenic varieties of rice (eg, basmati)§
- Avoid or limit use of rice milk or other rice beverages for infants‡ and children under 5 years old§,¶
- Read labels of processed foods: choose alternatives to foods sweetened with brown rice syrup or thickened with rice products[17]

4 Regulatory action

- Federal agencies should establish regulatory limits for arsenic content in rice and rice products§

*Adapted from various governmental and non-governmental organizations and scholarly articles.

†US FDA.[18]

‡AAP.[19,20,68]

§Consumer Reports.[8]

¶United Kingdom Food Standard Agency.[54]