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 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.

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

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

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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