A Holistic Look at Consumer Exposure to Lead, Cadmium and Arsenic, including Vulnerable Populations

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Overview

- Routes of exposure
- Background on occurrence and sources of heavy metals in the environment and diet
- Dietary exposure assessment
  - Objectives
  - Approaches
  - Data sources
  - Analysis considerations
- Current publicly available exposure estimates
- Risk management considerations
- Conclusions
Exposure assessment as a component of risk assessment

Risk Assessment Model
(source: EPA, 1992)
Exposure assessment: Heavy metals

- Lead, arsenic, cadmium are ubiquitous in our environment
- Multiple potential routes of exposure
  - Soil
  - Dust
  - Air
  - Drinking water
  - Food

(Source: Lead in the Environment Infographic | Lead | CDC)
Contribution of exposure pathways to total lead exposure among children 0-2 years of age (Source: Zartarian et al 2017)
OCCURRENCE AND SOURCES OF METALS
Arsenic

- Arsenic (As) occurs in the environment from natural and anthropogenic sources
  - Can be found in rocks, soil, and natural ground water.
  - Occurs in a wide variety of foods, including rice, vegetables, fruit and fruit juices.

- Two primary forms:
  - Organic (mostly non-toxic)
  - Inorganic (toxic) – typically present in natural ground water

- Primary exposure is food and drinking water among children (entering the food chain through water and/or soil) (EFSA 2014, ATSDR 2007).

- FDA has issued guidance on inorganic arsenic levels in apple juice and infant rice cereal
Cadmium

- Found in the earth’s crust.

- Can be emitted to the soil, water, and air through mining, manufacturing/application of fertilizers, fossil fuel combustion, and waste.

- Mobility in soil depends on factors such as pH and amount of organic matter.

- Cadmium binds to organic matter and can be taken up by plants. Tobacco leaves accumulate high levels of cadmium from the soil and the primary route of exposure to cadmium among smokers.

- Among non-smokers, primary exposure to cadmium is from the food supply including leafy vegetables, potatoes, grains, legumes and seeds.
Lead

• Found in ore deposits; widely distributed around the world
• Anthropogenic sources include
  • Leaded gasoline (banned in 1995),
  • Debris and dust from deteriorating lead paint from older housing (pre-1978).
• Lead pipes/soldered joints
• Mining/smelting of ore, manufacturing of lead-containing products, manufacturing and application of lead-containing pesticides, fossil fuel combustion, and waste incineration
• Primary exposure among non-smoking adults is from food and water.
• Primary exposure among children is from surface dusts and is intensified by the hand-to-mouth activity.
• FDA has issued guidance and information on lead in pottery, vitamins, wine, candy, and juices for children.
DIETARY EXPOSURE TO HEAVY METALS
Uses of dietary exposure estimates

- Provide estimates of background dietary exposure
- Monitor the impact of regulatory actions
- Identify and quantify potential health hazards
- Provide support for international food standards and risk assessments

**Formula:**

\[
\text{Consumption rate of food} \times \text{Level of contaminant in food} = \text{Estimated daily intake}
\]

**Comparison:**

Compare intake to safety threshold or relevant toxicological dose (e.g. RfD)
History of dietary exposure to lead, arsenic, and cadmium

- Metal contaminants in food, particularly food eaten by infants and children, have been a major focus for decades among regulatory authorities.
- Ubiquitous in the environment due to natural occurrence and/or result of environmental pollution.
- Found in air, water, and soil where they can be taken up by plants and incorporated into the foods we consume.
- Regulatory agencies have long acknowledged this dietary route of exposure and have set action levels, exposure limits safety recommendations, maximum levels, etc.
Modeling a dietary exposure assessment

• Simple model but implementation can be complex
• Does it ask the right questions
  • What will the assessment be used for?
    • Premarket approval
    • Post market issues
    • Labeling
    • Research
    • Priority setting
  • What is the toxicological concern and who is the vulnerable subpopulation?
• Do we want to be conservative or precise?
• What data do we have?
Data Sources

1. Dietary Consumption Surveys
   - NHANES 1999-2018
   - WHO Cluster diets
   - Private surveys
   - Custom surveys

2. Contaminant Data
   - FDA TDS/TEP
   - WHO/ Global Environment Monitoring System (GEMS)
   - Manufacturer/Industry
   - Literature
Analysis considerations

• Derive estimates for:
  • *Per capita vs. per user* (consumers only)
  • Vulnerable subpopulations
  • Typical consumer (average, median) or high consumer (upper 90\textsuperscript{th} percentile), etc.

• Short term v usual intake:
  • Per eating occasion, 24-hr daily intake, N-day average intake, modeled usual longer-term intake

• On a g/day or g/kg bw/day basis

• Precision of the estimate
## Published estimates of dietary exposure to lead, arsenic, and cadmium

<table>
<thead>
<tr>
<th>Metal</th>
<th>Population</th>
<th>Mean/Median</th>
<th>Upper percentile</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lead (µg/day)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-6 y</td>
<td>1.2-3.2</td>
<td>2.0-4.6&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Spungen 2019</td>
<td></td>
</tr>
<tr>
<td>1-3 y</td>
<td>1.0-3.0</td>
<td>1.8-4.4</td>
<td>Spungen 2019</td>
<td></td>
</tr>
<tr>
<td>4-6 y</td>
<td>1.3-3.4</td>
<td>2.1-4.8</td>
<td>Spungen 2019</td>
<td></td>
</tr>
<tr>
<td><strong>Inorganic arsenic (µg/kg bw/day)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1 y</td>
<td>0.23 (food)</td>
<td>0.53 (food)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Xue et al 2010; <a href="#">JECFA 2011b</a></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.014 (water)</td>
<td>0.05 (water)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-2 y</td>
<td>0.10 (food)</td>
<td>0.29 (food)</td>
<td>Xue et al 2010; <a href="#">JECFA 2011b</a></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.03 (water)</td>
<td>0.15 (water)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3-5 y</td>
<td>0.08 (food)</td>
<td>0.21 (food)</td>
<td>Xue et al 2010; <a href="#">JECFA 2011b</a></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.04 (water)</td>
<td>0.15 (water)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cadmium (µg/kg bw/day)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-6 y</td>
<td>0.41</td>
<td>0.66</td>
<td>Spungen 2019</td>
<td></td>
</tr>
<tr>
<td>1-3 y</td>
<td>0.43</td>
<td>0.70</td>
<td>Spungen 2019</td>
<td></td>
</tr>
<tr>
<td>4-6 y</td>
<td>0.38</td>
<td>0.59</td>
<td>Spungen 2019</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> 90<sup>th</sup> percentile

<sup>b</sup> JECFA estimates were provided on mean weekly body weight basis; µg/day estimates were calculated from µg/kg bw/week by multiplying by the default bodyweight (bw) provided in the JECFA assessment (JECFA 2011a) and dividing by 7 days/week.

<sup>c</sup> 95<sup>th</sup> percentile
Contribution of food sources to dietary exposure to heavy metals among children

• Need to consider both amount of food consumed and levels of metals in the food

• The highest contributor to exposure is not necessarily from the foods with the highest metal content
  • For example, the highest contributor to lead exposure among children >1 year of age are among fruits, vegetables, dairy, and mixtures.
  • Many of the foods within those categories have non-detectable levels of lead (<5 ppb)

Data source: Spungen 2019; FDA Closer to Zero, November 2021 public meeting.
Heavy metals are ubiquitous in our environment and our food supply.

Generally, cannot point to any single food or food group as the primary source of dietary exposure.

Level of metals in any single food or food group is low.

Goal is to minimize risk.

- Recent FDA draft action level for lead in juices focused on potential reduction in dietary exposure to lead among children.

- Many nutritious foods contain these metals – cannot consider in isolation.
Recommendations that infants and toddlers consume a variety of foods

**Healthy U.S. Style Dietary Pattern: Toddlers Ages 12 Through 23 Months Who Are No Longer Receiving Human Milk or Infant Formula**

<table>
<thead>
<tr>
<th>FOOD GROUP OR SUBGROUP</th>
<th>700</th>
<th>800</th>
<th>900</th>
<th>1,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vegetables (cup eq/day)</td>
<td>1/1</td>
<td>1/1</td>
<td>1/1</td>
<td>1/1</td>
</tr>
<tr>
<td>Dark-Green Vegetables (cup eq/wk)</td>
<td>1/1</td>
<td>1/1</td>
<td>1/1</td>
<td>1/1</td>
</tr>
<tr>
<td>Red and Orange Vegetables (cup eq/wk)</td>
<td>1/1</td>
<td>1/1</td>
<td>1/1</td>
<td>1/1</td>
</tr>
<tr>
<td>Beans, Peas, Lentils (cup eq/wk)</td>
<td>1/1</td>
<td>1/1</td>
<td>1/1</td>
<td>1/1</td>
</tr>
<tr>
<td>Starchy Vegetables (cup eq/wk)</td>
<td>1/1</td>
<td>1/1</td>
<td>1/1</td>
<td>1/1</td>
</tr>
<tr>
<td>Other Vegetables (cup eq/wk)</td>
<td>1/1</td>
<td>1/1</td>
<td>1/1</td>
<td>1/1</td>
</tr>
<tr>
<td>Fruits (cup eq/day)</td>
<td>1/1</td>
<td>1/1</td>
<td>1/1</td>
<td>1/1</td>
</tr>
<tr>
<td>Grains (ounce eq/day)</td>
<td>1/1</td>
<td>2/1</td>
<td>2/1</td>
<td>3</td>
</tr>
<tr>
<td>Whole Grains (ounce eq/day)</td>
<td>1/1</td>
<td>2/1</td>
<td>2/1</td>
<td>2</td>
</tr>
<tr>
<td>Refined Grains (ounce eq/day)</td>
<td>1/1</td>
<td>1/1</td>
<td>1/1</td>
<td>1/1</td>
</tr>
<tr>
<td>Dairy (cup eq/day)</td>
<td>1/1</td>
<td>1/1</td>
<td>1/1</td>
<td>1/1</td>
</tr>
<tr>
<td>Protein Foods (ounce eq/day)</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

**Protein Foods Subgroups in Weekly Amounts**

- Meats, Poultry (ounce eq/wk): 8/1, 7, 7, 7/4
- Eggs (ounce eq/wk): 2, 2/1, 2/1, 2/1
- Seafood (ounce eq/wk): 2/3, 2/3, 2/3, 2/3
- Nuts, Seeds, Soy Products (ounce eq/wk): 1, 1, 1/1, 1/1
- Oils (grams/day): 9, 9, 8, 13
Public health impact

- Many of the foods that contribute to exposure also provide essential nutrients such as iron and zinc

- Arsenic in rice example:
  - Consumption of brown rice (and intake of nutrients found within, including folate, iron, and fiber) is associated with reduced risk of several chronic disease outcomes
  - Infants and toddlers with dietary patterns that contain rice and non-rice cereal have significantly higher intakes of essential nutrients and lower intake of processed foods

### Action levels/maximum limits for metals in dietary sources in the US

<table>
<thead>
<tr>
<th>Metal</th>
<th>Source</th>
<th>Limit</th>
<th>Regulatory agency</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Food/bottled water</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lead</td>
<td>Bottled water</td>
<td>5 ppb</td>
<td>FDA</td>
</tr>
<tr>
<td>Lead</td>
<td>Apple juice/other juices</td>
<td>20 ppb/10 ppb</td>
<td>FDA (DRAFT Action Levels)</td>
</tr>
<tr>
<td>Lead</td>
<td>Candy</td>
<td>100 ppb</td>
<td>FDA</td>
</tr>
<tr>
<td><strong>Inorganic arsenic</strong></td>
<td>Infant rice cereal</td>
<td>100 ppb</td>
<td>FDA</td>
</tr>
<tr>
<td><strong>Inorganic arsenic</strong></td>
<td>Bottled water</td>
<td>10 ppb</td>
<td>FDA</td>
</tr>
<tr>
<td><strong>Inorganic arsenic</strong></td>
<td>Apple juice</td>
<td>15 ppb</td>
<td>FDA</td>
</tr>
<tr>
<td><strong>Cadmium</strong></td>
<td>Bottled water</td>
<td>5 ppb</td>
<td>FDA</td>
</tr>
<tr>
<td><strong>Drinking water</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lead</td>
<td>Drinking water</td>
<td>15 ppb</td>
<td>EPA</td>
</tr>
<tr>
<td>Arsenic</td>
<td>Drinking water</td>
<td>10 ppb</td>
<td>EPA</td>
</tr>
<tr>
<td>Cadmium</td>
<td>Drinking water</td>
<td>5 ppb</td>
<td>EPA</td>
</tr>
</tbody>
</table>
Examples of results from program efforts to reduce exposure to metals among US children

Source: Closer to Zero: Action Plan for Baby Foods | FDA
Conclusions

• Exposure to heavy metals among children results from numerous routes

• Dietary exposure assessment allows for:
  • Combination of data on amount of foods consumed with levels of metals in the foods
  • Identification of research and regulatory priorities
  • Estimation of the potential reduction in risk that can occur with action levels

• Need to consider the public health impact of regulating or warning on foods that also contribute to the nutritional needs of young children
Thank you!

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