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Childhood Diet & Arsenic Exposure: Interesting Clinical Cases

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Objectives

At the end of this case presentation, participants will be able to:

- Order and interpret the most appropriate laboratory tests to workup arsenic exposure
- Describe the differences in health risks between inorganic and organic arsenic
- List common dietary sources of both inorganic and organic arsenic
- Identify at least two national or local-level resources to help guide safe seafood consumption
PEHSU Case Conference

Seafood & Arsenic in a 6 y/o boy
Interesting Case in 2015

- MD called NW PEHSU- interpreting urinary arsenic lab results?
- 6 y/o boy with learning and motor delays
- Parents requested heavy metal testing for urine and blood
Preferred lab workup?
Different approach?
Initial Labs

- CBC, ferritin, vitamin D, TSH, electrolytes, BUN/creat and spot urine and blood heavy metal testing
- Basic screening labs = unremarkable
- Serum heavy metal labs = unremarkable
## Initial Labs

### Random urine sample, Quest Lab

<table>
<thead>
<tr>
<th>Result Name</th>
<th>Value</th>
<th>Ref Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine, Random Urine</td>
<td>68.7 mg/dL</td>
<td>(2.0-149.0 -)</td>
</tr>
<tr>
<td>Arsenic, Random Urine</td>
<td>93 mcg/gm Cr</td>
<td>(&lt; 51 -)</td>
</tr>
<tr>
<td>Mercury, Random Urine</td>
<td>-</td>
<td>(&lt; 5 -)</td>
</tr>
<tr>
<td>Lead, Random Urine</td>
<td>-</td>
<td>(&lt; 10 -)</td>
</tr>
</tbody>
</table>
How do we know whether this level of arsenic is high for a child, or not?
How do we know whether this level of arsenic is high for a child, or not?

A: Compare to NHANES percentiles
## Urinary Total Arsenic (creatinine corrected) (2011 - 2012)

Geometric mean and selected percentiles of urine concentrations (in µg As/g of creatinine) for the U.S. population from the National Health and Nutrition Examination Survey.

<table>
<thead>
<tr>
<th>Survey years</th>
<th>Geometric mean (95% conf. interval)</th>
<th>50th (95% confidence interval)</th>
<th>75th (95% confidence interval)</th>
<th>90th (95% confidence interval)</th>
<th>95th (95% confidence interval)</th>
<th>Sample size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>11-12</td>
<td>7.77 (6.85-8.81)</td>
<td>6.39 (5.57-7.24)</td>
<td>13.7 (11.5-16.5)</td>
<td>30.8 (24.6-38.6)</td>
<td>50.4 (38.2-70.1)</td>
</tr>
<tr>
<td><strong>Age group</strong></td>
<td></td>
<td></td>
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<tr>
<td>6-11 years</td>
<td>11-12</td>
<td>8.63 (7.26-10.3)</td>
<td>6.87 (5.84-8.00)</td>
<td>12.3 (9.58-15.5)</td>
<td>27.7 (17.7-57.7)</td>
<td>91.2 (26.2-129)</td>
</tr>
<tr>
<td>12-19 years</td>
<td>11-12</td>
<td>5.75 (4.49-7.36)</td>
<td>4.69 (3.70-5.73)</td>
<td>8.73 (6.26-13.3)</td>
<td>22.1 (11.5-62.6)</td>
<td>34.9 (21.1-159)</td>
</tr>
<tr>
<td>20 years and older</td>
<td>11-12</td>
<td>8.04 (7.07-9.14)</td>
<td>6.52 (5.88-7.69)</td>
<td>14.8 (12.1-18.8)</td>
<td>32.4 (25.2-39.8)</td>
<td>49.7 (38.2-70.1)</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>11-12</td>
<td>7.20 (6.15-8.43)</td>
<td>6.13 (5.16-7.23)</td>
<td>12.5 (10.5-15.2)</td>
<td>28.3 (20.2-34.9)</td>
<td>50.4 (33.3-69.6)</td>
</tr>
<tr>
<td>Females</td>
<td>11-12</td>
<td>8.35 (7.40-9.42)</td>
<td>6.64 (6.12-7.37)</td>
<td>15.0 (12.2-19.1)</td>
<td>33.1 (26.1-41.4)</td>
<td>50.7 (39.8-79.0)</td>
</tr>
<tr>
<td><strong>Race/ethnicity</strong></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Mexican Americans</td>
<td>11-12</td>
<td>8.00 (6.85-8.36)</td>
<td>6.91 (6.07-7.98)</td>
<td>11.9 (9.05-14.6)</td>
<td>25.1 (16.7-39.4)</td>
<td>40.8 (24.0-70.1)</td>
</tr>
<tr>
<td>Non-Hispanic blacks</td>
<td>11-12</td>
<td>7.24 (5.61-9.61)</td>
<td>5.83 (4.65-7.96)</td>
<td>13.5 (9.02-19.0)</td>
<td>28.8 (21.5-46.3)</td>
<td>55.4 (31.6-87.1)</td>
</tr>
<tr>
<td>Non-Hispanic whites</td>
<td>11-12</td>
<td>7.13 (6.05-8.39)</td>
<td>5.72 (5.05-6.70)</td>
<td>12.4 (10.3-15.4)</td>
<td>28.4 (21.7-37.5)</td>
<td>46.5 (33.1-75.8)</td>
</tr>
<tr>
<td>All Hispanics</td>
<td>11-12</td>
<td>8.53 (7.74-9.40)</td>
<td>7.60 (6.84-8.42)</td>
<td>12.8 (11.2-14.1)</td>
<td>25.3 (20.8-30.8)</td>
<td>37.5 (28.2-50.6)</td>
</tr>
<tr>
<td>Asians</td>
<td>11-12</td>
<td>22.3 (19.1-26.1)</td>
<td>20.1 (16.3-25.2)</td>
<td>39.4 (32.2-51.0)</td>
<td>100 (73.2-129)</td>
<td>162 (114-202)</td>
</tr>
</tbody>
</table>

**Blomonitoring Summary:** [http://www.cdc.gov/biomonitoring/Arsenic_BiomonitoringSummary.html](http://www.cdc.gov/biomonitoring/Arsenic_BiomonitoringSummary.html)

**Factsheet:** [http://www.cdc.gov/biomonitoring/Arsenic_FactSheet.html](http://www.cdc.gov/biomonitoring/Arsenic_FactSheet.html)
Interpretation

Random urinary arsenic high compared to NHANES data, putting him over the 95th percentile.

This total urinary arsenic will reflect recent arsenic exposure from the past 1-2 days.
In the setting of a potential chronic exposure (i.e. not an acute poisoning), is it most useful to order a urinary arsenic, serum arsenic, or hair/nail sample arsenic?
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A serum (blood) arsenic level reflects arsenic exposure in the past: 1-2 hours

A urine arsenic level reflects arsenic exposure in the past: 1-2 days
Lab Options

- Hair and nail samples
  - **Not recommended**
  - Would reflect exposure in past 6-12 months, poor at detecting low levels
What does the total arsenic level tell us about what types of arsenic are present?
What does the total arsenic level tell us about what types of arsenic are present?

A: Trick question, it doesn’t really. It includes both inorganic and organic forms.
Total arsenic ($\text{As}_{\text{total}}$) composed of organic, inorganic, and arsine gas forms

- Organic (plants, animals)- arsenic combined with carbon and hydrogen; generally not toxic
- Inorganic (soil, water)- arsenic combined with oxygen, chlorine, and sulfur; more toxic
Interpretation

Total arsenic measures both inorganic and organic components = can be misleading
Food Sources

Rice, apples, fish/shellfish, seaweed, poultry, mushrooms.
Nonfood Sources (inorganic)

- Water
- Soil
- Pesticides/herbicides
- Lumber (pressure treated w/ copper chromated arsenate- CCA)
- Occupational
- Industrial pollution
- Tobacco/cigarette smoke
- Historical
What questions could a clinician ask to gather more information about potential arsenic sources/exposures?
What questions could a clinician ask to gather more information about potential arsenic sources/exposures?

A: Dietary history. Also nonfood sources.
In this case, how could you workup whether the dietary arsenic exposure was organic or inorganic?

A: Gather a dietary hx/typical food intake and habits.

1) Seafood = abstain from seafood for 2 days/48 hours, then redraw a total random urine arsenic.

2) No seafood, = order a speciated urinary arsenic to break out organic vs. inorganic.
An exposure history was gathered by the MD.

There were no nonfood arsenic exposures identified by the parents.

Direct questioning reveals that child is “picky” eater, but regularly eats “a lot of fish in various sources, mostly fried and some in sushi”

Family ate a fish-abstaining diet for 2 days and then followed up with a repeat urine sample.
### Subsequent Labs
*(After Abstaining from Seafood x48hrs)*

<table>
<thead>
<tr>
<th>Result Name</th>
<th>Value</th>
<th>Ref Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine, Random Urine</td>
<td>59.6 mg/dL</td>
<td>(2.0-149.0 - )</td>
</tr>
<tr>
<td><strong>Arsenic, Random Urine</strong></td>
<td>11 mcg/gm Cr</td>
<td>(&lt; 51 - )</td>
</tr>
<tr>
<td>Mercury, Random Urine</td>
<td>4 mcg/gm Cr</td>
<td>(&lt; 5 - )</td>
</tr>
<tr>
<td>Lead, Random Urine</td>
<td>See Comment</td>
<td>(&lt; 10 - )</td>
</tr>
</tbody>
</table>
Interpretation

- Arsenic levels after abstaining from seafood improved, now between the 50th and 75th percentiles
Any different approaches?
Routes of exposure

- Ingestion (food, water, soil)
- Inhalation (sawdust and smoke from CCA-treated wood)
- Dermal absorption (handling CCA wood)
Health Effects of Arsenic - Acute High Doses

- Abd pain, n/v/d
- Neuro & cardiovascular effects (ex. bruising (2° blood vessel damage), ↓ production RBCs & WBCs = fatigue, abnormal heart rhythm)
- Hepatic dysfunction
- Shock, encephalopathy, death (adult- single dose 60,000 mcg)
Health Effects of Arsenic- Chronic High Dose

- Months to years for sx to manifest
- Most studies at arsenic levels far above drinking water standard (ex. 100+ ppb daily)
  - Skin lesions
  - Peripheral neuropathy
  - GI, neuro, & cardio affects, anemia/pancytopenia, DM,
  - Possible decreased IQ or neurocognitive impairment in children
  - Cancer (skin, bladder, lung CA = strong; liver, kidney CA = limited)
What about health effects from arsenic levels at or below drinking water standard?

- ???
Health Effects of Arsenic

- Pregnancy/breastfeeding-
  - Crosses placenta, low levels in breastmilk
  - Low birth weight, fetal malformations, fetal death [in animal studies]
Treatment

- Identify and remove arsenic sources
- Good nutrition.
- No chelation (reserved for acute high-dose intoxication).
- If acute poisoning- look up.
Prevention & Counseling

Food:

Eat a varied diet focusing on a wide variety of whole unprocessed foods (esp. fruits and vegetables, preferably organic) and diversify grains.
A few notes on rice…

- Consider limiting rice consumption (CR max: adults 1-3 servings of rice or rice-based foods per week, children 1.25 servings per week or 1 small serving rice cereal/day).
- Choose lower-arsenic varieties of rice.
- Rinse rice and cook rice in extra water.
- Do not give infants rice cereal as their first solid food.
Avoid processed foods.

- If needed, buy processed foods that don’t contain rice (low-arsenic grains include barley, faro, couscous, bulgur wheat; to avoid gluten, amaranth, buckwheat, millet, quinoa, oats*, cornmeal, grits, polenta).
- Watch for rice syrup as a ‘natural’ sweetener.

Do not use rice milk as a dairy substitute for cow's milk.
A few notes on rice…

American Academy of Pediatrics (AAP) now suggests considering:

1. “Cereals from other grains, finely chopped meats, and vegetable purees are equally acceptable as rice cereal for introduction as first food”

2. Alternative thickeners like oats and cornstarch to thicken first foods (if needed, ex. reflux)
Prevention & Counseling

Nonfood:

- Test well water
- Avoid cigarette and tobacco smoke
- Wash hands and toys, and wet mop/dust your home often.
- Don’t use or burn CCA-treated wood
Prevention & Counseling

- Seal arsenic treated lumber with an oil-based sealant (annually)
- Do not allow your children to play on or around CCA-treated wood structures
- Do not garden in or around wood structures containing CCA
- Do not allow children to play in soil if it contains high levels of arsenic
- Avoid UV exposure/use sunscreen (b/c combined skin CA role w/ arsenic)
Regulation

- Drinking & bottled water = 10 ppb (EPA)
- Air = no regulation (EPA)
- Food = no enforceable regulation (FDA)
  - Non-binding “action level” of 10 ppb for apple juice
  - No maximum levels of arsenic for other foods (ex. rice, processed foods)
What else was going on?

• Being worked up for autism spectrum disorders…

• Close ongoing management and support for parents and children

• Worthwhile to repeat a urine arsenic (again, after 48 hr seafood abstaining diet; or ideally, even 1-2 weeks) in a few months to make sure levels were staying down
Case Teaching Moment

- Since dietary patterns/fish consumption were brought up in relationship to arsenic, good teaching moment with the family to talk about healthy fish consumption (maximize benefits, minimize risks)- this would touch on the issue of mercury as well
Readings


Readings

- Seafood Health Facts: Making Smart Choices (Balancing the Benefits and Risks of Seafood Consumption): Resources for Healthcare Providers and Consumers
Readings

Healthy Fish Consumption:

• http://www.fda.gov/food/foodborneillnesscontaminants/metals/ucm393070.htm
• http://www.doh.wa.gov/CommunityandEnvironment/Food/Fish/HealthyFishGuide
• http://www.doh.wa.gov/CommunityandEnvironment/Food/Fish/WomenandChildren
• http://www.doh.wa.gov/CommunityandEnvironment/Food/Fish/MercuryAdvisories
Readings

• FDA Arsenic in Rice and Rice Products:
  [http://www.fda.gov/Food/FoodborneIllnessContaminants/Metals/ucm319870.htm](http://www.fda.gov/Food/FoodborneIllnessContaminants/Metals/ucm319870.htm)

• FDA Arsenic in Apple Juice:
  [http://www.fda.gov/Food/FoodborneIllnessContaminants/Metals/ucm280209.htm](http://www.fda.gov/Food/FoodborneIllnessContaminants/Metals/ucm280209.htm)
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