Discussion of Research Recommendations: DRIs for Water, Potassium, Sodium, Chloride, and Sulfate

Dietary Reference Intake Research Synthesis Workshop


IOM Panel on Water and Electrolytes

LARRY J. APPEL chair
Johns Hopkins University,
Baltimore, MD
DAVID H. BAKER
University of Illinois, Champaign-Urbana
* ODED BAR-OR
McMaster University, Hamilton, ON
KENNETH L. MINAKER
Massachusetts General Hospital &
Harvard Medical School, Boston
R. CURTIS MORRIS, JR
University of California, San Francisco
* LAWRENCE M. REBNICK
New York Presbyterian Hospital &
Cornell University Medical College
MICHAEL N. SAWKA
U.S. Army Research Institute of
Environmental Medicine, Natick, MA
STELLA L. VOLPE
University of Pennsylvania, Philadelphia
MYRON H. WEINBERGER
Indiana University School of Medicine, Indianapolis
PAUL K. WHELTON
Tulane University Health Sciences Center, New Orleans
ALLISON A. YATES
Study Director (from June 2003)
PAUL R. TRUMBO
Study Director (through May 2003)

* Deceased
Outline

- Summary of DRIs
- Specific Research Recommendations
  - Sodium and Potassium, Water, Sulfate
- Other Issues
  - DRI Taxonomy
  - Evidence-Based Medicine and Nutrition Policy
  - General (Research) Issues

DRI Summary

<table>
<thead>
<tr>
<th></th>
<th>Al</th>
<th>UL</th>
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<tbody>
<tr>
<td>Water</td>
<td>2.7 L / d (W)</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>3.7 L / d (M)</td>
<td>None</td>
</tr>
<tr>
<td>Sodium</td>
<td>65 mmol / d</td>
<td>100 mmol / d</td>
</tr>
<tr>
<td>Potassium</td>
<td>120 mmol / d</td>
<td>None</td>
</tr>
<tr>
<td>Sulfate</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

Rationale for UL

- Sodium
  - Lower blood pressure
### Rationale for AI

**Rationale**

**Water**
- Median observed in NHANES III

**Sodium**
- Nutrient adequacy
- Buffer in setting of excess sodium loss during acute thermal stress

**Potassium**
- Lower blood pressure
- Reduce salt sensitivity
- Reduce risk of kidney stones
- Decrease bone loss

### Water

### Hypothesized Adverse Effects of Inadequate Water Intake

- Chronic Illness
  - Cancers
    - Bladder
    - Colon
  - Urologic conditions
    - Kidney stones
    - Urinary tract infection
  - Ischemic Heart Disease

- Dehydration
  - Reduced cognitive function
  - Reduced physical function
  - Biomarker
    - Serum or plasma osmolality

- Hypothized Adverse Effects
  - Dehydration
  - Chronic illness
  - Urologic conditions
    - Kidney stones
    - Urinary tract infection
  - Ischemic Heart Disease

- Dehydration
  - Reduced cognitive function
  - Reduced physical function
  - Biomarker
    - Serum or plasma osmolality
### Mean Serum Osmolality in 1st, 5th and 10th Deciles of Daily Total Water Intake in Men and Women (NHANES III)

<table>
<thead>
<tr>
<th>Age</th>
<th>Decile</th>
<th>Water Intake, L/day</th>
<th>Serum Osmolality (mOsm/kg)</th>
<th>Water Intake, L/day</th>
<th>Serum Osmolality (mOsm/kg)</th>
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<tbody>
<tr>
<td>19–50 y</td>
<td>1st</td>
<td>1.69</td>
<td>279</td>
<td>1.25</td>
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<tr>
<td></td>
<td>5th</td>
<td>3.31</td>
<td>280</td>
<td>2.61</td>
<td>277</td>
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<tr>
<td></td>
<td>10th</td>
<td>7.93</td>
<td>280</td>
<td>6.16</td>
<td>277</td>
</tr>
<tr>
<td>51–70 y</td>
<td>1st</td>
<td>1.84</td>
<td>280</td>
<td>1.32</td>
<td>281</td>
</tr>
<tr>
<td></td>
<td>5th</td>
<td>3.17</td>
<td>283</td>
<td>2.66</td>
<td>281</td>
</tr>
<tr>
<td></td>
<td>10th</td>
<td>7.20</td>
<td>281</td>
<td>5.81</td>
<td>279</td>
</tr>
<tr>
<td>71+ y</td>
<td>1st</td>
<td>1.44</td>
<td>283</td>
<td>1.19</td>
<td>282</td>
</tr>
<tr>
<td></td>
<td>5th</td>
<td>2.71</td>
<td>283</td>
<td>2.38</td>
<td>283</td>
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<tr>
<td></td>
<td>10th</td>
<td>5.45</td>
<td>281</td>
<td>4.85</td>
<td>282</td>
</tr>
</tbody>
</table>

### Potassium

#### Hypothesized Adverse Effects of Inadequate Potassium Intake

- Hypothesized adverse effects
  - arrhythmias
  - insulin resistance
  - increased blood pressure
  - salt sensitivity
  - kidney stones
  - bone turnover
- Biomarker
  - serum potassium level
Potassium Blunts The Pressor Effects of Increased Salt Intake ('Salt Sensitivity')

Cross-over trial with 7 day periods

Salt sensitivity:

≥ 3 mmHg increase in response to a change in sodium intake from 0.7 to 5.8 g (30 to 250 mmol/day)

Morris, 1999

Relative Risk of Kidney Stones by Quintile of Potassium Intake in 45,619 Men (Curhan, 1993)

* P-trend < 0.001

Sodium Chloride (Salt)
Hypothesized Adverse Effects of Inadequate Sodium Intake

- Increased plasma renin activity
- Increased insulin resistance
- Adverse lipid changes
- Nutrient inadequacy
- Volume depletion in setting of acute thermal stress

Hypothesized Adverse Effects of Excess Sodium Intake

- Increased urinary calcium excretion
- Increased left ventricular mass
- Increased risk of gastric cancer
- Increased blood pressure

Sodium Dose Response Trials: Luft, 1979 (14 non-hypertensive)

<table>
<thead>
<tr>
<th>Sodium Dose (grams/day)</th>
<th>SBP (mm Hg)</th>
<th>DBP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.23 (10)</td>
<td>+1</td>
<td>+1</td>
</tr>
<tr>
<td>6.9 (200)</td>
<td>+2</td>
<td>+2</td>
</tr>
<tr>
<td>13.8 (600)</td>
<td>+2</td>
<td>+2</td>
</tr>
<tr>
<td>18.4 (800)</td>
<td>+4</td>
<td>+4</td>
</tr>
<tr>
<td>27.6 (1200)</td>
<td>+6</td>
<td>+6</td>
</tr>
<tr>
<td>34.5 (1500)</td>
<td>+7</td>
<td>+5</td>
</tr>
</tbody>
</table>

SBP (mm Hg): 0.23, 6.9, 13.8, 18.4, 27.6, 34.5
DBP (mm Hg): 0.23, 6.9, 13.8, 18.4, 27.6, 34.5

grams/day (mmol/day): 0.23, 6.9, 13.8, 18.4, 27.6, 34.5
Effect of Sodium Level on Systolic Blood Pressure (Sacks, 2001)

- Control Diet: +2.1
- DASH Diet: +1.3
- Sodium Level (mmol/d): 65, 100, 140
- Systolic Blood Pressure: 120, 125, 130, 135

Research Recommendations:

Sodium and Potassium

§ Develop effective public health strategies to achieve and sustain reduced sodium intakes and increased potassium intakes in the general population, including behavioral change studies in individuals and community-based intervention studies.

Ongoing activity: NHBLI, Great Britain, NYC Health Dept
Research Recommendation: Sodium & Potassium

Develop alternative processing technologies to reduce the sodium content of foods, with a special emphasis on maintaining flavor, texture, consumer acceptability, safety, and low cost.

Progress: proposal, investigator-initiated trial

Research Recommendation: Sodium & Potassium

Conduct trials that test the efficacy of increased potassium intake (alone and in combination with reduced sodium intake) on preventing stroke.

Progress: pilot studies underway

Research Recommendation: Sodium & Potassium

Conduct trials that test the main and interactive effects of potassium and sodium intake on bone mineral density and, if feasible, bone fractures.

Progress: proposal, investigator-initiated trial
Research Recommendation: Sodium & Potassium

β Conduct trials testing the main and interactive effects of sodium and potassium intake on the risk of kidney stones.

Progress: long-term (10-15 yr) of intervention trials documented ~20% reduced risk of CVD events (Cook, AHA abstract, 2004)

β Conduct a formal assessment of the feasibility of a large-scale, long-term clinical trial designed to assess the impact of sodium reduction on clinical cardiovascular outcomes.

β Investigate the influence of sodium intake during infancy and childhood on blood pressure later in life.
Research Recommendation: Sodium & Potassium

§ Conduct studies to assess the potential for increased potassium intake to mitigate the adverse consequences of excess sodium intake and, vice versa, the potential for a reduced sodium intake to mitigate the adverse consequences of inadequate potassium intake.

Research Recommendation: Sodium & Potassium

§ Conduct studies on the adverse effects of chronic, low-grade metabolic acidosis that results from an inadequate intake of potassium and its bicarbonate precursors.

Progress: pilot studies underway

Research Recommendation: Sodium & Potassium

§ Conduct randomized clinical trials to compare the effect of different potassium salts on blood pressure and other outcomes at different levels of sodium intake.

Progress: potassium citrate and chloride had similar effects on BP (He, Hypertension, 2005)
Research Recommendation: Sodium & Potassium

§ Develop better estimates of potassium losses in sweat with various dietary, activity, and environmental conditions in diverse populations.

Research Recommendation: Sodium & Potassium

§ Conduct trials to assess the effects of high potassium intake on serum potassium levels and blood pressure in the setting of early stages of renal insufficiency (with and without ACE [angiotensin converting enzyme] inhibitor therapy).

Research Recommendation: Sodium & Potassium

§ Investigate the main and interactive effects of sodium and potassium intake on the age-related rise in blood pressure.
Research Recommendation: Sodium & Potassium
§ Develop practical tools to measure intakes of sodium and potassium and to assess total body levels of sodium and potassium.

Research Recommendations: Water

Research Recommendation: Water
§ Investigate the effects of hydration status and fluid intake on the occurrence of urinary tract infections.
Research Recommendation: Water

β Investigate the effects of hydration status and fluid intake on chronic disease, such as kidney stones and gall stones (cholelithiasis), as well as the occurrence of specific cancers, including colon cancer and bladder cancer.

Research Recommendation: Water

β Conduct water, sodium, and potassium balance studies that enroll broad populations and that vary climate and physical activity levels.

Research Recommendation: Water

β Develop simple non- or minimal-invasive indexes of body hydration status (both hyperosmotic and isoosmotic).
Research Recommendation: Water

- Develop capabilities to predict hourly and daily water requirements based on metabolic rate, climatic conditions, and clothing for different subgroups of the population.

Research Recommendation: Water

- Validate estimates of total water intake, both from food and fluids, in large-scale surveys.

Research Recommendation: Water

- Investigate the effects of chronic overhydration, in the presence of adequate sodium intake, on health and cognitive ability.
Research Recommendations:
Sulfate

β Assess the relationship between increased sulfate intake and risk of inflammatory bowel disease.

β Investigate the effects of acute versus chronic sulfate ingestion on diarrhea as well as whether and at what point adaptation occurs.
Other Issues

DRI Taxonomy

- General issue: application of DRI model to chronic diseases
- Specific issues:
  - Adequate Intake (AI) - need to catalog approaches and consider revision to definition
  - Tolerable Upper Limit – difficulty to apply to direct, progressive relationships without a threshold

Conceptual Model Used to Develop Dietary Reference Intakes

- EAR, RDA, UL
- Observed level of intake
- Risk of inadequacy
- Risk of excess
- 0.5
- Intake per unit
Conceptual Model Used to Develop Dietary Reference Intakes

<table>
<thead>
<tr>
<th>Fraction below EAR</th>
<th>Fraction above UL</th>
</tr>
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<tbody>
<tr>
<td>0.5</td>
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<th>27.6</th>
<th>34.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP (mm Hg)</td>
<td>+4</td>
<td>+2</td>
<td>+2</td>
<td>+4</td>
<td>+6</td>
<td></td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>+1</td>
<td>+5</td>
<td>+2</td>
<td></td>
<td></td>
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</table>
Evidence-Based Medicine and Nutrition Policy

- Major impediments to nutrition-intervention trials with clinical outcomes (virtually none with several doses)
- Use of surrogate outcomes for nutrition policy is inevitable, yet criteria and process for selecting surrogate outcomes is ill-defined

General (Research) Issues

- DRI for infants, children, pregnant women, elderly
- Adjustment factors: calories, weight, age, gender
- What is ‘healthy’, especially given high probability of subsequently developing chronic diseases?
- What should be the process for prioritizing research recommendations?