In summary, based on evidence from both humans and animal models, we believe that plant sterol levels in plasma are not related to increased CHD risk.

Vanu Ramprasath, PhD
Peter J. H. Jones, PhD
Jiri Frohlich, MD

Author Affiliations: Richardson Center for Functional Foods and Nutraceuticals, University of Manitoba, Winnipeg, Canada (Dr Ramprasath and Jones); and Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, Canada (Dr Frohlich).

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr Jones reported receiving grants from the Canadian Institutes of Health Research (CIHR), Canada Research Chair Endowment (CRCE) of the Federal Government of Canada, Advanced Foods and Materials Network (AFM Net), Danone, Enzymotec, and Unilever. Dr Jones also serves as president of Nutritional Fundamentals for Health, which markets plant sterols among other nutraceuticals. Dr Ramprasath reported receiving grants from CRCE of the Federal Government of Canada, CIHR, AFM Net, Loblaw Brands, Solae, and Unilever. Dr Frohlich reported no disclosures.


RESEARCH LETTER

Canned Soup Consumption and Urinary Bisphenol A: A Randomized Crossover Trial

To the Editor: Human exposure to bisphenol A (BPA) is widespread. In adults, urinary BPA concentrations are positively associated with cardiovascular disease and diabetes.

Exposure occurs primarily through the diet. Bisphenol A has been quantified in many canned goods, where it is present as a by-product of interior epoxy coatings used to prevent corrosion. We hypothesized that canned soup consumption would increase urinary BPA concentrations relative to fresh soup consumption.

Methods. In 2010, we recruited Harvard School of Public Health (HSPH) student and staff volunteers (aged >18 years) via informational fliers and e-mail. The study was approved by the HSPH institutional review board. Written informed consent was obtained.

We used a randomized, single-blinded, 2 × 2 crossover design. For the first 5-day period (October 25-29, 2010), one group consumed a 12-ounce serving of fresh soup (prepared without canned ingredients) daily between 12:15 and 2 PM; the other group consumed a 12-ounce serving of canned soup (from 18.5-ounce Progresso brand) per the same schedule. After a 2-day washout, treatment assignments were reversed (November 1-5, 2010). We used 5 different

2218 JAMA, November 23/30, 2011—Vol 306, No. 20
©2011 American Medical Association. All rights reserved.
varieties of vegetarian soup per treatment and repeated them in the same order the following week. Participants were not restricted in their consumption of other foods.

Donation of spot urine samples took place between 3 and 6 PM on the fourth and fifth days of each phase. Urine was collected in polyethylene containers and stored in polypropylene cryogenic vials. When urine was donated both days, combined urine samples were created to minimize within-person variation. The specific gravity (SG) of the urine was measured using a handheld refractometer; total (free plus conjugated species) urinary BPA concentration was measured at the Centers for Disease Control and Prevention using online solid-phase extraction coupled to isotope dilution high-performance liquid chromatography–tandem mass spectrometry.6

Urinary BPA concentrations were adjusted for dilution by multiplying values (in µg/L) by [(1.014−1)/(SG−1)]. In the absence of a period effect, we used a paired t test to examine mean absolute change in SG-adjusted untransformed urinary BPA concentrations (BPA_{canned}−BPA_{fresh}) because differences were normally distributed, and we calculated confidence intervals for the mean using SAS version 9.2. Statistical tests were 2-sided and performed at the .05 level of significance.

Results. Of 84 volunteers, 75 (89%) completed the study. Median age was 27 years and 51 (68%) were female; median treatment adherence was 100% (TABLE). Bisphenol A was detected in 77% (n=58) of samples after fresh soup consumption and 100% (n=75) of samples after canned soup consumption. The SG-adjusted geometric mean concentration of BPA was 1.1 µg/L (95% CI, 0.9-1.4 µg/L) after fresh soup consumption (unadjusted: 0.9 µg/L; 95% CI, 0.7-1.2 µg/L) and 20.8 µg/L (95% CI, 17.9-24.1 µg/L) after canned soup consumption (unadjusted: 17.5 µg/L; 95% CI, 14.1-21.8 µg/L). Stratification by treatment sequence revealed similar values (FIGURE). Following canned soup consumption, SG-adjusted urinary BPA concentrations were, on average, 22.5 µg/L higher (95% CI, 19.6-25.5 µg/L) than those measured after a week of fresh soup consumption (P<.001), representing a 1221% increase.

Comment. Consumption of 1 serving of canned soup daily over 5 days was associated with a more than 100% increase in urinary BPA. Generalizability is limited due to selection of participants from 1 school and testing of a single soup brand; however, generalizability to canned goods with similar BPA content is expected. The increase in urinary BPA concentrations following canned soup consumption is likely a transient peak of yet uncertain duration. The effect of such intermittent elevations in urinary BPA concentration is unknown. The absolute urinary BPA concentrations observed following canned soup consumption are among the most extreme reported in a nonoccupational setting. For comparison, the 95th percentile unadjusted urinary BPA in the 2007-2008 National Health and Examination Survey was 13.0 µg/L (95% CI, 10.0-15.4 µg/L).1 The observed increase in urinary BPA concentrations following canned soup consumption, even if not sustained, may be important, especially in light of available or proposed alternatives to epoxy resins linings for most canned goods.

Jenny L. Carwile, MPH
Xiaoyun Ye, MS
Xiaoliu Zhou, MS
Antonia M. Calafat, PhD
Karin B. Michels, ScD, PhD

Author Affiliations: Department of Epidemiology, Harvard School of Public Health, Boston, Massachusetts (Ms Carwile); National Center for Environmental Health, Centers for Disease Control and Prevention, Atlanta, Georgia (Ms Ye and Zhou and Dr Calafat); and Obstetrics and Gynecology Epidemiology Center, Harvard Medical School, Boston (Dr Michels) (kpmichels@rics.bwh.harvard.edu).

Author Contributions: Ms Carwile had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Table. Characteristics of 75 Participants in Crossover Study of Changes in Urinary Bisphenol A Concentrations Associated With Daily Consumption of Canned Soup

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>24 (32.0)</td>
</tr>
<tr>
<td>Female</td>
<td>51 (68.0)</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>39 (52.0)</td>
</tr>
<tr>
<td>Asian</td>
<td>21 (28.0)</td>
</tr>
<tr>
<td>Black</td>
<td>8 (10.7)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>6 (8.0)</td>
</tr>
<tr>
<td>Other</td>
<td>1 (1.3)</td>
</tr>
<tr>
<td>Age, median (range), y</td>
<td>27 (22-56)</td>
</tr>
<tr>
<td>Adherence, median (range), %</td>
<td>100 (60-100)</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Self-reported race/ethnicity was categorized by the investigators and assessed for the purpose of informing generalizability to other populations.

Adherence was calculated as the percentage of days that a participant consumed assigned soup.

Figure. Geometric Mean Specific Gravity–Adjusted Urinary Bisphenol A Concentration After a Week of Soup Consumption by Treatment Sequence

Geometric mean specific gravity (SG)–adjusted urinary bisphenol A (BPA) concentration following a week of daily consumption of fresh or canned soup. For reference, the unadjusted geometric mean for the 2007-2008 National Health and Examination Survey (NHANES) was 2.08 µg/L (95% CI, 1.92-2.26 µg/L), and the 95th percentile was 13.0 µg/L (95% CI, 10.0-15.4 µg/L). Error bars indicate 95% CIs.

©2011 American Medical Association. All rights reserved.
Study concept and design: Carwile, Michels.
Acquisition of data: Carwile.
Analysis and interpretation of data: Carwile, Michels.
Drafting of the manuscript: Carwile.
Critical revision of the manuscript for important intellectual content: Carwile, Ye, Zhou, Calafat, Michels.
Statistical analysis: Carwile.
Obtained funding: Michels.
Administrative, technical, or material support: Carwile, Ye, Zhou, Calafat.
Study supervision: Michels.
Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.
Funding/Support: This project was supported by an Allen Foundation grant to Dr Michels. Ms Carwile was supported by a Training Grant in Environmental Epidemiology (T32 ES 007069) from the National Institute of Environmental Health Sciences.
Role of the Sponsor: The sponsors had no role in the design and conduct of the study; in the collection, analysis, and interpretation of the data; or in the preparation, review, or approval of the manuscript.
Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention. The involvement of the Centers for Disease Control and Prevention (CDC) was limited and was determined not to constitute engagement in human subjects research.
Additional Contributions: We thank Lori Torf of the Harvard School of Public Health cafeteria for assistance with soup preparation and distribution; Martin Breslin of the Harvard Dining Services for providing the freshly prepared soups; Nikita Jambulingam (Harvard College) for assistance with data collection; and Lily Jia, MS, and Ryan Hennings (National Center for Environmental Health, Centers for Disease Control and Prevention) for technical assistance in measuring urinary BPA. None of the individuals acknowledged were compensated for the contributions.


CORRECTION
Incorrect Number: In the Original Contribution entitled “Association Between Smoking and Risk of Bladder Cancer Among Men and Women,” published in the August 17, 2011, issue of JAMA (2011;306[7]:737-745), an incorrect number was reported in Table 2. Under the column for Women, Person-Years and in the row Former smoker (overall), the number should be 705,925 (not 70,595). This article was corrected online.

Late on the third day, at the very moment when, at sunset, we were making our way [by boat] through a herd of hippopotamuses, there flashed upon my mind, unforeseen and unsought, the phrase, “Reverence for Life.” The iron door had yielded: the path in the thicket had become visible. Now I had found my way to the idea in which affirmation of the world and ethics are contained side by side! Now I knew that the ethical acceptance of the world and of life, together with the ideals of civilization contained in this concept, has a foundation in thought.

—Albert Schweitzer (1875-1965)