Evidence Development and Standards Branch at Health Quality Ontario

Special Report

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Testing for Blood Mercury Levels in the General Population

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Context

Mercury is a naturally occurring element. When exposed to high levels of mercury, individuals can suffer serious health effects. Although clinically significant exposures still occur in Canada, a large proportion of individuals who present with concerns of metal toxicity do not have true poisoning.

Research Question

What are the indications, if any, for measuring mercury levels in the general population?

Conclusion

- Mean total blood mercury levels ranged from 0.58 µg/L to 4.15 µg/L across 6 studies.
- Predictors of higher blood mercury levels included: fish consumption (6/6 studies), dental amalgams (3/6 studies), age (3/6 studies), race/ethnicity (2/6 studies), education level (1/6 studies), alcohol consumption (2/6 studies), smoking status (1/6 studies), and gender (1/6 studies).
- There were no indications for the participants in these studies to be at high risk for toxic blood mercury concentrations based on their exposures. The mean total blood mercury concentrations were substantially lower than the Health Canada guidance values, suggesting that even among those persons with environmental exposure to mercury, metal toxicity will be rare.

Methodology

Research questions are developed by Choosing Wisely Canada, in consultation with experts, end users, and/or applicants in the topic area. Evidence Development and Standards then produces one of two types of rapid reviews, or a special report to answer the research question. A rapid review of Systematic Reviews is conducted when a systematic literature search identifies relevant systematic reviews, health technology assessments, or meta-analyses that meet the inclusion criteria specified in the methods section. A rapid review of primary studies is conducted when none of the aforementioned study designs are available. On occasion, a special report may be provided that does not strictly follow the rapid review methodology set out by HQO. These reports are completed in a 2- to 8-week time frame. For more detail on rapid review methodology, please visit the Health Quality Ontario website at: http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations/rapid-reviews.

Context

Choosing Wisely Canada is a national campaign that aims to help physicians and patients engage in informative conversations about tests, treatments, and procedures, and help physicians and patients make smart and effective choices to ensure high-quality care. It will support physicians as they work with patients to ensure they not only get the care they need, but avoid tests, treatments, and procedures that have no value and could cause them harm.

As part of this campaign, Health Quality Ontario (HQO) has developed rigorous, evidence-based reviews of tests, treatments, and/or procedures that may be overused. Choosing Wisely Canada has made recommendations based on the evidence provided by HQO. These recommendations are available on the Choosing Wisely Canada website.

Objective of Rapid Review

The objective of this analysis was to evaluate the indications for measuring mercury levels in the general population.

Clinical Need and Target Population

Description of Disease/Condition

Mercury is a naturally occurring element that can exist in three forms: elemental (or metallic), inorganic (with exposure coming primarily through a person's occupation), and organic (e.g., methylmercury, with exposure coming through diet). Previous studies have shown that inorganic mercury comprises 14% to 26% of total blood mercury in adults. (1-3) All humans are exposed to some level of mercury, usually at low levels that cause no physical symptoms. However, when exposed to high levels of mercury, the lungs, kidneys, skin, and eyes and the nervous, digestive, and immune systems can be effected, dependent on the form of mercury, the dose, age of the person, and the duration and route of exposure. (4)

For adults, Health Canada's guidance value for total blood mercury concentrations is 8 µg/L for women of child-bearing age, and 20 µg/L for females ≥ 50 years and males > 18 years. (5) Although clinically significant exposures still occur in Canada, a large proportion of individuals who present with concerns of metal toxicity do not have true poisoning (6). According to the Canadian Health Measures Survey (CHMS), less than 1% of Canadian adults have total blood mercury concentrations above Health Canada's guidance value. (5)

Technology/Technique

In clinical laboratories, physicians can test for mercury levels through samples of blood, urine, and hair. Blood tests are generally used to measure the organic form of mercury (methylmercury) because of the high rate of uptake of methylmercury in red blood cells. Urine tests obtain a good sample for assaying elemental and inorganic mercury. However, the urine test for organic mercury is not a reliable indicator of the level of organic mercury in the body.

In Ontario, according to 2009/2010 hospital data, 7,741 mercury tests were ordered in 2009 and 5,541 tests in 2010. (Data Source: Laboratory Licensing – June 2012) According to 2009/2010 and 2010/2011 community data, 5,577 mercury tests were ordered in 2009/2010 costing $85,848 dollars. In 2010/2011,

4,958 mercury tests were ordered costing $79,573 dollars. (Data Source: OSRS, OHIP Statistical Reporting System M7 – June 2012).

For the purpose of this review, the focus is narrowed to adults within the general population who have been exposed to organic and inorganic mercury as measured by blood tests.

Question, Methods, and Findings

Research Question

What are the indications, if any, for measuring mercury levels in the general population?

Methods

See Appendix 1 for a detailed description of the search strategy, including terms and results.

Inclusion Criteria

- English-language full-text publications
- published between January 1, 2002, and July 24, 2014
- observational studies, randomized controlled trials (RCTs), systematic reviews, and meta-analyses
- adult population
- sample representative of general population

Exclusion Criteria

- paediatric and animal studies
- hair and urine tests to measure blood mercury levels

Outcomes of Interest

- total blood mercury levels
- factors associated with high blood mercury levels

Findings

The database search yielded 3,122 citations published between January 1, 2004, and July 24, 2014 (duplicates removed). Articles were excluded based on information in the title and abstract. The full texts of potentially relevant articles were obtained for further assessment.

No systematic reviews or meta-analyses examined the total blood mercury levels in the general population, but 6 observational studies met the inclusion criteria. The reference lists of the included studies were hand-searched to identify other relevant studies, but no additional citations were included.

All the studies included were cross-sectional and the participants in these studies were meant to be representative of the general population for their respective countries. All studies examined factors associated with high blood mercury levels and reported the mean total blood mercury concentrations. However, Bjermo et al (7) reported the median Hg values separately for men and women.

Table 1 describes the objective, descriptive statistics of participants, how the relevant variables were measured, and factors *not* associated with high blood mercury levels of the included studies. Table 2 describes the results of the included studies.

Table 1: Objectives, descriptive statistics and how factors were measured in the Observational Studies Identified

Author, Year	Objective of Study	Descriptive Statistics of Sample Mean Age (SD)	Measures	Factors Not Associated With High Blood Mercury Levels
Becker et al, 2002 (8)	To examine cadmium, lead, mercury, and organochlorine compounds in whole blood to document the extent, distribution, and determinants of exposure of the general population to these substances	• Not reported • It is stated that the sample is representative of the German population in regards to age, gender, community size, and region	**Fish Consumption** • Measured by frequency of intake and categorized as: never, ≤ 1 per month, 2–3 per month, ≤ 1 per week, and > 1 per week **Dental Amalgams** • Measured by number of fillings and categorized as: 0, 1–4, 5–8, and >8	• Not reported
Mahaffey et al, 2004 (9)	To examine the association between dietary factors and blood mercury levels	• Not reported • Only women in this sample	**Fish Consumption** • Based on frequency of consumption in the last 30 days and categorized as: 0 times in 30 days (never), 1–4 times per month, 5–8 times per month, ≥ 9 times per month **Age** • Divided into 4 ranges: 16–19, 20–29, 30–39, and 40–49 years of age **Race/Ethnicity** • Categorized as: Mexican American, other Hispanic, Non-Hispanic white, Non-Hispanic black, and other	• Not reported
Gundacker et al, 2006 (10)	To determine causal factors underlying mercury exposure and to estimate the gender-related health impacts	• 44 years old (± 12) • 46% had a basic (elementary or secondary school) education level	**Fish Consumption** • Measured by frequency of intake and categorized as: never, occasional (≤ 1 per week), and frequent (> 1 per week). **Dental Amalgams** • Measured continuously by number of fillings	• Gender • Age • Education level
Kim and Lee, 2010 (11)	To examine the association between total blood mercury concentration and fish consumption in the Korean general adult population	• Not reported	**Fish Consumption** • Divided into 3 groups based on consumption: < 1 per week, 1 per week, and > 1 per week **Age** • Divided into 5 ranges: 20–29, 30–39, 40–49, 50–59, and 60 years and older **Alcohol Consumption** • Divided into 4 groups according to the average daily alcohol consumption:	• Regional distribution • Education level

Author, Year	Objective of Study	Descriptive Statistics of Sample Mean Age (SD)	Measures	Factors Not Associated With High Blood Mercury Levels
			nondrinker, light drinker (1–15 g per day), moderate drinker (16–30 g per day), and heavy drinker (>30 g per day)	
Bjermo et al, 2013 (7)	To examine body burden of mercury, lead, and cadmium in the blood of Swedish adults and the association between blood levels, diet, and other lifestyle factors	• Mean age of women and men in this sample were 48.2 ± 16.5 and 52.5 ± 17.0, respectively • The majority of women and men did not smoke (55% of women and 68% of men were nonsmokers) • 43% of women and 41% of men had education beyond high-school	**Fish Consumption** • Measured by frequency of intake and was categorized as: ≤ 1 per month, > 1 per month and > 1 per week **Age** • Measured continuously **Education** • Divided into three categories: elementary school, high-school, and higher education	• BMI • Energy intake • Smoking status • Regional distribution • Plasma ferritin
Lye et al, 2013 (12)	To assess total mercury in the blood and predictors of mercury in the blood of Canadians aged 6 to 79	• Approximately 34.2% of people in the sample were between the ages of 40 and 59 • Males made up half (50.2%) of the sample • The majority (75.9%) of people in the sample had a post-secondary education	**Fish Consumption** • Categorized based on consumption: never eats fish or shellfish, eats fish or shellfish < 1 time per week, 1 to < 3 times per week, and ≥ 3 times per week **Alcohol Consumption** • Categorized as: < 1 drink per week, 1 to 3 drinks per week, 4 to 6 drinks per week, daily drinking **Smoking Status** • Categorized as: current smoker, former smoker, and never smoked regularly **Dental Amalgams** • Categorized as: 0, 1–10, 11–25, and 26+ amalgams **Race/Ethnicity** • Categorized as: Caucasian, Asian, Aboriginal and other, or multiracial	• Income • Education level

Abbreviations: BMI, body mass index; SD, standard deviation.

Table 2: Results of the Observational Studies Identified

Author, Year Country Study Design	Survey	• Total Hg Geometric Mean (95% CI) • 95th Percentile *(See last column)*	Predictors of Hg in blood	Above HC Guidance Value (8 µg/L or 20 µg/L)[a]
Becker et al, 2002 (8) Germany N = 4,645 ***Cross-Sectional***	The German Environmental Survey (GerES III)	• 0.58 µg/L (0.57–0.60) • 2.3 µg/L	**Fish Consumption** • Participants who normally do not consume fish showed a GM of 0.29 µg/L, while persons with a fish consumption of more than once a week showed a GM of 0.91 µg/L ($P \leq 0.001$). **Dental Amalgams** • Participants who had no amalgam filling at all showed a mean Hg concentration of 0.50 µg/L (GM) and those with 1–4 teeth with amalgam had a concentration of 0.57 µg/L. For subjects with 5–8 and >8 teeth with amalgam, a concentration of 0.65 µg/L and 0.80 µg/L, respectively, was found (no *P* value provided).	• No
Mahaffey et al, 2004 (9) United States N = 1,707 (women) ***Cross-Sectional***	The National Health and Nutrition Examination Survey (NHANES)	• 1.02 µg/L (0.85–1.20) • 7.13 µg/L	**Fish Consumption** • Blood mercury concentrations were 7 times higher among women who reported eating nine or more fish and/or shellfish meals within the past 30 days (2.46 µg/L) than among women who reported no fish and/or shellfish consumption in the past 30 days (0.39 µg/L; $P \leq 0.0001$). **Age** • Blood organic/methylmercury concentrations were ~1.5 times higher among women 30–49 years of age (0.83 µg/L for 30–39 years of age and 1.02 µg/L for 40–49 years of age) than among women 16–29 years of age (0.49 µg/L for 16–19 years of age and 0.70 µg/L for 20–29 years of age; $P \leq 0.0001$) **Race/Ethnicity** • Blood organic/methylmercury concentrations were lowest among Mexican Americans (0.57 µg/L) and highest among participants who designated themselves in the other racial/ethnic category (1.06 µg/L), which includes Asians, Native Americans, and Pacific Islanders ($P \leq 0.028$)	• No

Author, Year Country Study Design	Survey	• Total Hg Geometric Mean (95% CI) • 95th Percentile *(See last column)*	Predictors of Hg in blood	Above HC Guidance Value (8 µg/L or 20 µg/L)[a]
Gundacker et al, 2006 (10) Austria N = 152 ***Cross-Sectional***	Not specified	• 2.38 µg/L (0.34–9.97) • Not reported	**Fish Consumption (Women and Men)** • Frequent (> 1 serving/week) fish consumption significantly influenced blood mercury concentrations in women and men (3.01 ± 1.96 µg/L; *P* < 0.05) • Occasional (≤ 1 serving/week) seafood (mussel and crustacean) consumption significantly influenced blood mercury concentrations in women (3.50 ± 2.51 µg/L and 3.60 ± 2.68 µg/L; *P* < 0.05) **Dental Amalgams (Men)** • Men with amalgam fillings showed significantly higher mercury levels (2.53 ± 1.51 µg/L) than those without fillings; this relationship was not significant in females (*P* < 0.05)	• No
Kim and Lee et al, 2010 (11) Korea N = 1,749 ***Cross-Sectional***	The Korean National Health and Nutritional Examination Survey (KHANES III)	• 4.15 µg/L (3.93–4.38) • Not reported	**Fish Consumption** • The geometric mean of the blood mercury level was significantly higher in the high fish-consumption group (4.38 µg/L; > 1 serving per week) than in the low-consumption group (3.71 µg/L: < 1 serving per week; *P* < 0.01). **Age** • The blood mercury level was significantly lower in the youngest age group (20–29 years) than in the 40–49 and 50–59 years age groups (*P* < 0.05) **Alcohol Consumption (Women)** • Heavy drinker (4.61 µg/L) participants had significantly higher blood mercury concentrations than nondrinkers (3.33 µg/L; *P* < 0.01)	• No
Bjermo et al, 2013 (7) Sweden N = 273 ***Cross-Sectional***	National Survey Riksmaten (subgroup)	• Median Hg value for women (5th–95th percentile): 0.97 µg/L (0.17–2.9) • Median Hg value for men (5th–95th percentile): 1.3 µg/L (0.39–4.4)	**Fish Consumption** • Fish consumption was positively related to blood mercury levels in a stepwise regression (mean% changes per gram per day, 0.88; SE = 0.12; *P* < 0.001) **Age** • Higher age (mean% increase per year, 1.9; SE = 0.3) was associated with higher blood mercury concentration (no *P* value provided)	• No

Author, Year Country Study Design	Survey	• Total Hg Geometric Mean (95% CI) • 95th Percentile *(See last column)*	Predictors of Hg in blood	Above HC Guidance Value (8 µg/L or 20 µg/L)[a]
			Gender • Male gender (mean% difference, 34.1; SE = 13.1) was associated with higher blood mercury concentration (no *P* value provided) **Education level** • More education (mean% change from lowest to highest education, 51.1; SE = 21.8) was associated with higher blood mercury concentration (no *P* value provided)	
Lye et al, 2013 (12) Canada N = 5,319 ***Cross-Sectional***	Canadian Health Measures Survey (CHMS)	• 0.69 µg/L (0.56–0.86) • 4.70 µg/L (2.61–6.78)	**Fish Consumption** • Participants who consumed no fish or shellfish (0.14 µg/L) had statistically significant lower blood mercury levels compared with participants who consumed fish and shellfish (0.48, 0.90, 1.90 µg/L, respectively), regardless of the frequency of consumption (*P* < 0.0001) **Alcohol Consumption** • Survey participants who consumed alcoholic drinks 4 to 6 times per week or more (1.07 µg/L) had statistically significantly higher blood mercury levels compared with those who reported drinking less than once a week (0.71 µg/L; *P* = 0.0002) **Smoking status** • Former (0.87 µg/L) and never smokers (0.75 µg/L) have significantly higher blood mercury levels compared to current smokers (0.58 µg/L; *P* < 0.01) **Dental Amalgams** • Participants with no dental amalgams (0.60 µg/L) had significantly lower mean blood mercury levels compared with participants who had 11-25 amalgams (0.88 µg/L) and with participants who had ≥ 26 amalgams (1.28 µg/L; *P* = 0.01) **Race/Ethnicity** • Mean blood mercury concentration was significantly higher in those participants who identified as “other or mixed” (1.14 µg/L) and Asians (1.41 µg/L) compared to Caucasians (0.62 µg/L; *P* = 0.02).	• No

Abbreviations: CI, confidence intervals; GM, geometric mean, HC, Health Canada, SE, standard error.

[a]8 µg/L for infants, children, and women of child-bearing age and 20 µg/L for females ≥ 50 years and males > 18 years of age.

Conclusions

- Mean total blood mercury levels in adults that participated in these studies ranged from 0.58 µg/L to 4.15 µg/L across 6 studies.
- Predictors of higher blood mercury levels in adults included: fish consumption (6/6 studies), dental amalgams (3/6 studies), age (3/6 studies), race/ethnicity (2/6 studies), education level (1/6 studies), alcohol consumption (2/6 studies), smoking status (1/6 studies), and gender (1/6 studies).
- The mean total blood mercury concentrations were substantially lower than the Health Canada guidance values, suggesting that even among those people with environmental exposure to mercury, metal toxicity will be rare.

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Appendices

Appendix 1: Research Methods

Literature Search Strategy

A literature search was performed on July 24, 2014, using Ovid MEDLINE, Ovid MEDLINE In-Process, all EBM Databases for studies published from January 1, 2002, to July 24, 2014. Abstracts were reviewed by a single reviewer and, for those studies meeting the eligibility criteria, full-text articles were obtained. Reference lists were also examined for any additional relevant studies not identified through the search.

Search Results

Search date: July 24, 2014
Librarians: Corinne Holubowich and Caroline Higgins
Databases searched: Ovid MEDLINE, Ovid MEDLINE In-Process, All EBM Databases (see below)

Database: EBM Reviews - Cochrane Database of Systematic Reviews <2005 to June 2014>, EBM Reviews - ACP Journal Club <1991 to July 2014>, EBM Reviews - Database of Abstracts of Reviews of Effects <2nd Quarter 2014>, EBM Reviews - Cochrane Central Register of Controlled Trials <June 2014>, EBM Reviews - Cochrane Methodology Register <3rd Quarter 2012>, EBM Reviews - Health Technology Assessment <2nd Quarter 2014>, EBM Reviews - NHS Economic Evaluation Database <2nd Quarter 2014>, Ovid MEDLINE(R) <1946 to July Week 3 2014>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <July 23, 2014>

#	Searches	Results
1	Environmental Exposure/ or maternal exposure/ or paternal exposure/	63269
2	Environmental Pollutants/ or Environmental Pollution/	37343
3	exp Mercury Poisoning/	4441
4	Mercury/ or Methylmercury Compounds/	23084
5	Food Contamination/ or Dental Amalgam/	38867
6	((mercury or methylmercury or methyl mercury or MeHg) adj2 (poison* or expos* or filling* or amalgam* or toxic* or vapo?r or consum*)).ti,ab.	5925
7	or/1-6	152036
8	exp Hematologic Tests/	219576
9	exp Mercury Poisoning/bl [Blood]	156
10	Mercury/bl, to [Blood, Toxicity]	3564
11	Methylmercury Compounds/bl, to [Blood, Toxicity]	1871
12	((mercury or methylmercury or methyl mercury or MeHg) adj2 (test* or blood or level*)).ti,ab.	3030
13	or/8-12	226849
14	7 and 13	7720
15	limit 14 to (english language and yr="2002 -Current") [Limit not valid in CDSR,ACP Journal Club,DARE,CLCMR; records were retained]	3435
16	Case Reports/ or Comment.pt. or Editorial.pt. or Letter.pt. or Congresses.pt.	2932844
17	15 not 16	3233
18	remove duplicates from 17	3122

Appendix 2: Evidence Quality Assessment

Evaluation of Evidence

The methodology for a rapid review of primary studies includes a risk of bias assessment based on GRADE Working Group criteria (13) to assess quality of evidence. Risk of bias is evaluated based on consideration of allocation concealment, binding, accounting of patients and outcome events, selective reporting bias, and other limitations (see Table A1).

Table A1: Risk of Bias Among Observational Trials for the Comparison of Predictors of Blood Mercury Levels

Author, Year	Appropriate Eligibility Criteria	Appropriate Measurement of Exposure(s)	Appropriate Measurement of Outcome	Adequate Control for Confounding	Complete Follow-Up
Becker et al, 2002 (8)	No limitations	Limitations[a]	No limitations[b]	No limitations[c]	Limitations[d]
Mahaffey et al, 2004 (9)	No limitations[e]	Limitations[a]	No limitations[b]	No limitations[f]	Limitations[g]
Gundacker et al, 2006 (10)	No limitations	Limitations[a]	No limitations[b]	No limitations[f]	Limitations[g]
Kim and Lee, 2010 (11)	No limitations	Limitations[a]	No limitations[b]	No limitations[f]	No limitations
Bjermo et al, 2013 (7)	No limitations	Limitations[a]	No limitations[b]	No limitations[f]	Limitations[g]
Lye et al, 2013 (12)	No limitations	Limitations[a]	No limitations[b]	No limitations[f]	Limitations[h]

[a]There may be recall bias as all of the studies included were cross-sectional.
[b]Appropriate protocols were followed to ensure quality samples.
[c]Variables are controlled for when conducting an analysis of covariance (ANCOVA).
[d] The response rate was 55% and a sensitivity analysis indicated that non-responders were different on certain variables (education, etc).
[e]Only women were included in this study, so not representative of males.
[f]Variables are controlled for when conducting regression analysis.
[g]The authors did not state the response rate for this sample.
[h]The overall response rate was slightly above 50%, and no sensitivity analysis was conducted to examine if non-responders were systematically different than participants.

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Conflict of Interest Statement

All authors in the Evidence Development and Standards branch at Health Quality Ontario are impartial. There are no competing interests or conflicts of interest to declare.

Disclaimer

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Health Quality Ontario is an arms-length agency of the Ontario government. It is a partner and leader in transforming Ontario's health care system so that it can deliver a better experience of care, better outcomes for Ontarians, and better value for money.

Health Quality Ontario strives to promote health care that is supported by the best available scientific evidence. The Evidence Development and Standards branch works with expert advisory panels, clinical experts, scientific collaborators, and field evaluation partners to conduct evidence-based reviews that evaluate the effectiveness and cost-effectiveness of health interventions in Ontario.

Based on the evidence provided by Evidence Development and Standards and its partners, the Ontario Health Technology Advisory Committee—a standing advisory subcommittee of the Health Quality Ontario Board—makes recommendations about the uptake, diffusion, distribution, or removal of health interventions to Ontario's Ministry of Health and Long-Term Care, clinicians, health system leaders, and policy-makers.

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To create its CWC reports, the Evidence Development and Standards branch and its research partners review the available scientific literature, making every effort to consider all relevant national and international research and solicit any necessary supplemental information.

In addition, Evidence Development and Standards collects and analyzes information about how a health intervention fits within current practice and existing treatment alternatives. Details about the diffusion of the intervention into current health care practices in Ontario add an important dimension to the review. Information concerning the health benefits, economic and human resources, and ethical, regulatory, social, and legal issues relating to the intervention may be included to assist in making timely and relevant decisions to optimize patient outcomes.

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