

## Evaluation of Mercury in Urine as an Indicator of Exposure to Low Levels of Mercury Vapor

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We conducted a pooled analysis to investigate the relationship between exposure to elemental mercury in air and resulting urinary mercury levels, specifically at lower air levels relevant for environmental exposures and public health goals (i.e., < 50  $\mu\text{g}/\text{m}^3$  down to 1.0  $\mu\text{g}/\text{m}^3$ ). Ten studies reporting paired air and urine mercury data (149 samples total) met criteria for data quality and sufficiency. The log-transformed data set showed a strong correlation between mercury in air and in urine ( $r = 0.774$ ), although the relationship was best fit by a series of parallel lines with different intercepts for each study ( $R^2 = 0.807$ ). Predicted ratios of air to urine mercury levels at 50  $\mu\text{g}/\text{m}^3$  air concentration ranged from 1:1 to 1:3, based on the regression line for the studies. Toward the lower end of the data set (i.e., 10  $\mu\text{g}/\text{m}^3$ ), predicted urinary mercury levels encompassed two distinct ranges: values on the order of 20  $\mu\text{g}/\text{L}$  and 30–60  $\mu\text{g}/\text{L}$ . Extrapolation to 1  $\mu\text{g}/\text{m}^3$  resulted in predicted urinary levels of 4–5 and 6–13  $\mu\text{g}/\text{L}$ . Higher predicted levels were associated with use of static area air samplers by some studies rather than more accurate personal air samplers. Urinary mercury predictions based primarily on personal air samplers at 1 and 10  $\mu\text{g}/\text{m}^3$  are consistent with reported mean (4  $\mu\text{g}/\text{L}$ ) and upper-bound (20  $\mu\text{g}/\text{L}$ ) background levels, respectively. Thus, although mercury levels in air and urine are correlated below 50  $\mu\text{g}/\text{m}^3$ , the impact of airborne mercury levels below 10  $\mu\text{g}/\text{m}^3$  is likely to be indistinguishable from background urinary mercury levels. **Key words:** air exposure, background urinary mercury levels, mercury vapor, pooled analysis, urinary mercury. *Environ Health Perspect* 111:623–630 (2003). [Online 30 October 2002] doi:10.1289/ehp.5717 available via <http://dx.doi.org/>

Public exposures to low levels of mercury have received increased attention as a result of past ubiquitous uses and releases of this metal, improved analytical detection methods, and a growing public awareness of the sources and health effects of mercury exposure (ATSDR 1999; Clarkson 2002). Much of this concern has focused on the organic form of mercury (methyl mercury) in the environment (FDA 2001; NRC 2000). However, the elemental (metallic) form of mercury can also affect the central nervous system and, like organic mercury, may be a concern for developmental effects in children (ATSDR 1999). Although dental amalgams are the primary source of elemental mercury exposure in the general population, releases of this metal from consumer products and devices (e.g., thermometers, barometers, thermostats, electrical switches, fluorescent lights, gas pressure regulators, batteries, and use of older latex paint) can also contribute to public exposures (Agocs et al. 1990; Aronow et al. 1990; ATSDR 1999, 2000; Zeitz et al. 2002).

In response to concerns about mercury vapor exposure in homes, schools, or businesses due to accidental releases from removal of gas-pressure regulators, ATSDR (2000) established a “residential occupancy level” of 1.0  $\mu\text{g}/\text{m}^3$  for elemental mercury in ambient air that was considered safe for occupants (ATSDR 2000) and protective of health, even

of sensitive populations chronically exposed to mercury vapor.

Some public health agencies have also recommended biomonitoring of inhabitants in those homes where mercury has been detected above certain benchmark air concentrations (IDPH 2001; Renninger 2000). The concentration of mercury in urine is considered the most accurate biomarker for understanding the absorbed dose from chronic exposure to mercury vapor, whereas blood mercury levels are considered more appropriate for evaluating short-term or peak exposures (ATSDR 1999; Barregård 1993; Fiserova-Bergerova et al. 2000). Unlike mercury in blood, urinary mercury levels are less affected by methyl mercury exposure from the diet (ATSDR 1999). However, dietary mercury exposure from high fish consumption may contribute to urinary mercury levels (Abe et al. 1995; Suzuki et al. 1993).

The average background concentration of mercury in urine has often been reported to be about 4  $\mu\text{g}/\text{L}$  in the general population, with an upper bound (e.g., 95th percentile) of about 20  $\mu\text{g}/\text{L}$  (ATSDR 1999; Iyengar and Woittiez 1988; Minoia et al. 1990; Skerfving 1972; WHO 1990, 1991), although considerable variation is apparent in studies reporting background urinary mercury levels in subgroups from different locations and in those that report urinary mercury measurements for control or unexposed groups in

nonoccupational or occupational settings (Table 1). More recent studies reporting levels specifically for pediatric populations have means and often upper-bound values generally well below 3  $\mu\text{g}/\text{L}$  (Table 1).

Many studies have also found a strong correlation between the level of mercury in urine and the level of elemental mercury in air in occupational settings where exposures are relatively high (Ehrenberg et al. 1991; Nordhagen et al. 1994; Roels et al. 1987; Schaller and Triebig 1984; Stopford et al. 1978). Less understood is whether exposures at much lower airborne mercury levels (i.e., 1–10  $\mu\text{g}/\text{m}^3$ ) can be detected in urine above background levels. In fact, some reports note a lack of correlation between air and urine mercury levels at airborne concentrations < 50  $\mu\text{g}/\text{m}^3$  (ATSDR 1999; Lindstedt et al. 1979). The relationship between urine and air mercury at low levels has been difficult to assess in most studies because of inadequate data in this range of air concentrations.

We conducted a quantitative analysis of the published literature in an attempt to determine if biological monitoring of mercury in urine can be used to evaluate low-level airborne exposures to elemental mercury. In particular, we evaluated whether exposures to 1–10  $\mu\text{g}/\text{m}^3$  of elemental mercury in air will result in changes in urinary mercury levels that can be distinguished from background. Data from 10 studies were interpreted using pooled analysis techniques.

### Methods

We reviewed the literature for published articles containing air and urine mercury concentration data. More than 20 articles that contained air and urine mercury data for individuals or groups were identified.

**Study inclusion criteria.** Many studies identified in the literature contained insufficient data or information to include in the

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combined analysis or lacked controls for variables that affect the accuracy of urine or air mercury measurements. We used several criteria for deciding which studies to include in the analysis:

- 1) Studies must contain multiple paired airborne and urinary mercury concentration data that are representative of the same time period and location of exposure.
- 2) Subjects of studies should have chronic exposure to airborne mercury (i.e., at least 6 months based on the time for mercury in urine to reach steady state with exposure to mercury vapor) (ACGIH 2000).
- 3) Air measurements should be collected over most of a day [preferably averaged over several days to ameliorate high reported variation in day-to-day exposures of workers (Symanski et al. 2000)] and should be expressed as a time-weighted average (TWA).
- 4) Urine data should be expressed as an average of multiple spot samples per individual or as an average of urinary data from several individuals.
- 5) Urine samples should be collected using standard collection procedures or based on

a structured approach (e.g., all samples collected at a certain time of the day).

- 6) Urine should be corrected or normalized for hydration state (unless the sample is a composite over most of the day).
- 7) Air concentration data should preferably include measurements  $< 50 \mu\text{g}/\text{m}^3$ .

All studies included in our analysis met at least criteria 1, 3, and 4 (Table 2). We included some studies that did not meet all of the criteria if they were judged to be of sufficient quality and fulfilled most of the criteria. For example, three studies (Mattiussi et al. 1982; Nordhagen et al. 1994; Smith et al. 1970) lacked details on how or when urine samples were collected. Three studies also did not mention the length of worker employment (Bell et al. 1973; Mattiussi et al. 1982; Muller et al. 1980). Because all of these are occupational investigations, however, they likely used a standard approach for urine collection and were based on chronic exposures (i.e., greater than 6 months).

Studies that clearly did not meet the more important criteria 1–4 were excluded from the combined analysis. For example, several case

reports involving persons exposed to high levels of mercury vapors indoors either did not provide airborne mercury measurements or reported air concentration data based on unrepresentative (i.e., grab) samples (Agocs et al. 1990; Blair et al. 1989; Mortensen et al. 1990; Sasso et al. 1996). Other studies included unpaired air and urine data based on a single air and/or urine measurement per individual or data for multiple individuals presented as a single summary (i.e., average) measure (Cianciola et al. 1997; Ehrenberg et al. 1991; Fawer et al. 1983; Hudson et al. 1987; Ishihara et al. 1977; Joselow et al. 1968; Lauwerys and Buchet 1973; Nakaaki et al. 1975; Sällsten and Barregård 1997; Schaller and Triebig 1984; Schuckmann 1979; Stewart et al. 1977; Yang et al. 1994). One controlled experimental study (Nakaaki et al. 1975) was found, but the exposure period was relatively short (4–5 hr per day for 3–14 days). These studies were not included in the pooled analysis.

**Correction of urinary data.** Most of the included studies reported urinary mercury levels based on spot samples or first-morning

**Table 1.** Reported urinary background levels of mercury in general population and unexposed workers.

Study population	n	Mean ( $\mu\text{g}/\text{L}$ )	Range ( $\mu\text{g}/\text{L}$ )	Reference
Adults/general population				
Unexposed male chloralkali workers (controls) in the United States and Canada	142	NR	< 10 (35%); 10–100 (63%) 110–300 (2%)	Smith et al. (1970)
Persons from 15 countries providing baseline data	1,107	NR	< 0.5 (79%); < 5.0 (86%) < 10 (89%); < 20 (95%)	Skerfving (1972)
Female nurses in Kenya (controls) never using skin creams with mercury	17	2	ND–20	Barr et al. (1973)
Male and female biological laboratory technicians (controls)	23	2.30 <sup>a</sup>	1.49 <sup>a</sup> (SE)	Lauwerys and Buchet (1973)
Male and female workers (controls) in histopathology laboratory	21	10 <sup>b,c</sup>	ND–22 <sup>c</sup>	Stewart et al. (1977)
Unexposed workers (controls) in a heat sensor manufacturing plant	5	9.0 <sup>d</sup>	4–15 <sup>d</sup>	Stopford et al. (1978)
Norwegian residents in more industrial area, less industrial area	240, 103	7.4, 4	0.4–42, 0.6–24	Lie et al. (1982)
Male workers (controls) in fluorescent tube and chemical production plants	25	6.0 <sup>a</sup>	1.24 <sup>a</sup> (SE)	Fawer et al. (1983)
Workers (controls) in “mercury free” plants in Belgium: males, females	114, 48	0.9 <sup>a</sup> , 1.7 <sup>a</sup>	0.1–4.9 <sup>a</sup> , 0.1–4.9 <sup>a</sup>	Roels et al. (1985)
Adults from 55 countries providing baseline data on mercury	7	4.3 <sup>b</sup>	0.1–20	Iyengar and Woitiez (1988)
Male workers (controls) in wood processing plants: study I, study II	41, 60	1.8 <sup>a</sup> , 2 <sup>a</sup>	ND–5.03 <sup>a</sup> , ND–6 <sup>a</sup>	Piikivi (1989); Piikivi and Hanninen (1989)
Residents of 10 homes with nonmercurial paint in Michigan	28	1.9 <sup>a,b</sup>	0.04–7.0 <sup>a</sup>	Agocs (1990)
Healthy residents in northern Italy	380	3.5	0.1–6.9	Minoia et al. (1990)
Male adults with no history of occupational exposure to mercury in Japan	87	2.8	0.5–15	Yamamura (1990)
Electronic instrument manufacturing workers (controls)	70	4.2 <sup>a</sup>	2.3 <sup>a</sup> (SD)	Ehrenberg et al. (1991)
Male workers (controls) in government agency, park forest, and fire station	29	5.0 <sup>b</sup>	2.6–11.6	Hefflin et al. (1993)
New York adults: with fillings, without fillings	66, 34	1 <sup>b</sup> , < 0.25 <sup>b</sup>	< 0.25–23, < 0.25–10	Eti et al. (1995)
Male teachers of chemistry lab, nonchemistry classes in Ohio	12, 9	4.6 <sup>a,b</sup> , 6.3 <sup>a,b</sup>	2.2–8.2 <sup>a</sup> , 2.7–19.0 <sup>a</sup>	Crump et al. (1996)
Residents near inactive mine in California: tribal members, nontribal members	51, 5	1.7, 0.7	0.4–12.5, 0.2–2.4	Harnly et al. (1997)
Reference population of children and adults in Russia	380	NR	< 0.1–40, $\leq 2$ (90%)	Pogarev et al. (1997)
Unexposed “referents” for a chloralkali plant in Sweden	40	3.5 <sup>a</sup>	0.9–9 <sup>a</sup>	Sällsten and Barregård (1997)
Czech adults	1,192	1.33 <sup>a</sup>	0.06–9.0 <sup>a</sup> , $\leq 3.79^a$ (95%)	Beneš et al. (2002)
Children				
Children (controls) of nonmercury plant workers in Vermont	39	5.0 <sup>b</sup>	< 1–< 20	Hudson et al. (1987)
Norwegian children (12 years old)	73	1.0 <sup>a</sup>	$\leq 2.8^a$ (95%)	Olstad et al. (1987)
Japanese children (age 3–18 years): boys, girls	556, 1,086	2.4, 2.7	2.0, 2.5 (SD)	Suzuki et al. (1993)
Turkish children (age 4–12 years) after amalgam restoration	10	0.59	0.34–1.7, 0.401 (SD)	Ulukapi et al. (1994)
Japanese children (age 0–4 years): boys, girls	57, 58	1.67, 2.78	1.06, 3.31 (SD)	Tsuda et al. (1995)
East German children (age 5–14 years)	803	0.36 <sup>a,e</sup>	0.03–13.9 <sup>a</sup>	Trepka et al. (1997)
Inner city New York children (mean age 9.4 years)	100	1.08	$\leq 2.8$ (95%)	Ozuah et al. (2000)
Iranian children (age 5–7 years): before, after dental amalgam filling	43	3.83 <sup>d</sup> , 5.14 <sup>d</sup>	2.54 <sup>d</sup> , 3.14 <sup>d</sup> (SD)	Khordi-Mood et al. (2001)
Czech children (mean age 9.9 years)	2,008	0.93 <sup>a</sup>	0.06–18 <sup>a</sup> , $\leq 3.02^a$ (95%)	Beneš et al. (2002)

Abbreviations: ND, nondetected value; NR, not reported.

<sup>a</sup>Converted from micrograms per gram of creatinine to micrograms per liter assuming an average creatinine level of 1 g/L. <sup>b</sup>Median. <sup>c</sup>Converted from nanomoles per 24 hr to micrograms per liter assuming 1.4 L/day urine output. <sup>d</sup>Reported as adjusted for specific gravity. <sup>e</sup>Geometric mean.

voids rather than 24-hr urine collections. To account for the variation in mercury concentration of a urine sample due to differences in hydration, the mercury urine concentration is usually corrected to a standard hydration state. The most common correction method used in these studies was to adjust the urine mercury concentration in micrograms per liter to a common specific gravity. Where possible, we selected data normalized to a specific gravity of 1.024. In a few cases (Table 2), the data were either normalized to other specific gravity values or unspecified values, were uncorrected for hydration state, or were corrected by expressing the amount of mercury per amount of urinary creatinine (micrograms per gram creatinine). Results expressed in units of micrograms per gram creatinine were converted to units of micrograms per liter by assuming an average amount of creatinine in urine of 1 g/L (Boeniger et al. 1993).

**Evaluation of data sets.** A total of 10 studies meeting the above criteria were combined for analysis of air and urine mercury levels (Table 2). Data from the two Lindstedt et al. (1979) studies were analyzed as separate studies because of differences in air concentrations and sample collection methodology. All 10 studies were of mercury-exposed workers in facilities such as chloralkali and thermometer-manufacturing plants. Mercury concentrations in ambient air were based

(about equally) on personal and static area monitoring samples, whereas most urinary mercury levels were based on averages of spot samples from individual workers. Although some of the data reported in these studies relate to mercury air exposure levels of 50  $\mu\text{g}/\text{m}^3$  or greater, data were also available for much lower air concentrations. Seven studies had data in the range of 3–25  $\mu\text{g}/\text{m}^3$ , for a total of 52 data points in this range (Table 3).

Mattiussi et al. (1982), Muller et al. (1980), and the two studies by Lindstedt et al. (1979) reported raw numerical data for mercury in air and urine. Data from the other studies in the combined analysis were reported in graphical form only. Consequently, these data were scanned using computer imaging techniques to obtain the numerical concentrations of mercury in air and urine. These data should therefore not be interpreted as precise quantitative estimates, although the amount of error introduced from scanning the data appears to be relatively small based on comparison of the linear regression equation we derived to that reported by some of the studies (Table 4).

Table 4 includes the subset of studies that reported regression results, regardless of how we obtained the data. The study by Ehrenberg et al. (1991) was excluded from the pooled analysis because it did not meet the inclusion criteria, but it is presented here for illustrative

purposes. For studies in which the data were scanned, the previously reported slopes were well within the 95% confidence interval of that calculated from the digitized data. For the studies that did not require digitizing, we obtained virtually the same result (i.e., correlation coefficient, slope, and intercept) for Mattiussi et al. (1982), but not for the two Lindstedt et al. (1979) studies. Because Lindstedt et al. (1979) reported the raw data, this difference is not due to inaccuracies in imaging the data but may be due to differences in statistical methods or reporting errors.

Although all studies included in our analysis assessed the air mercury to urine mercury relationship using non-log-transformed data, the variance of the individual and combined data sets was highly dependent on the mean (i.e., the higher the mean, the higher the variance; Figure 1). The data were thus log-transformed for statistical analysis to satisfy the homogeneity of variance assumption underlying the regression (sums-of-square) analysis. Log transformation greatly reduced the nonhomogeneity of variance (Figure 2). A recent regression analysis of variation in airborne and biologic mercury concentrations in workers also used log-transformed data (Symanski et al. 2000).

After analyzing the combined data set, we grouped data on individual worker means of

**Table 2.** Studies and data used in analysis of relationship between air and urine mercury levels.

Study	Air methods/data	Urine methods/data <sup>a</sup>	Study characteristics (data source) <sup>b</sup>	Inclusion criteria met
Bell et al. (1973)	Personal samples; 8 hr over 5 days (TWA)	16-hr composite sample on Friday	Four individual composites each from distinct job classes, in mercury cell plant manufacturing chlorine (Figure 1; study I). Study II reported as less reliable.	1, 3, 4–6
Lindstedt et al. (1979) Study I	Static samples; daily for 2 weeks (TWA)	Spot samples (not SG corrected) daily (postshift) for 2 weeks	Thirteen individual means in a chloralkali plant (Figure 2)	1–4, 6, 7
Lindstedt et al. (1979) Study II	Personal samples; daily for 8 weeks (TWA)	Spot samples twice a week for 8 weeks (postshift)	Fifteen individual means in chloralkali plant (Figure 3)	1–6
Mattiussi et al. (1982)	Static samples over 1–3 years (TWA) reported as identical to personal sampling	Sample type and duration not specified	Twenty-one group means of 275 workers from nine job classes in five chloralkali plants (Figure 1)	1, 3, 4, 6, 7
Muller et al. (1980)	Personal samples for 8–9 hr over 10 days (TWA)	Four samples (SG corrected = 1.017) over a day (morning/home, preshift, midshift, postshift)	Fifteen individual means of cellroom operators (five per plant) in three NaCl electrolysis plants (Table 1)	1–7
Nordhagen et al. (1994)	Static samples; twice a week at 130 points. Annual means 1953–1987 based on quarterly means	Quarterly samples (type and SG correction not reported)	Thirty-four group annual averages of 419 workers in four job classes of a chloralkali plant study (Figure 4)	1–4, 7
Roels et al. (1987)	Personal samples; 6 hr over 5 days (TWA)	9 A.M. spot samples for 5 days <sup>c</sup>	Ten individual means of two to four samples matched to previous day's TWA sample from a distinct work area in dry alkaline battery plant (Figures 2, 4, 5)	1–7
Smith et al. (1970)	Static samples collected six times a year (TWA)	Unspecified sample type four times per year	Eighteen group means of 560 workers in 21 chloralkali plants (Figure 5)	1–4, 7
Stopford et al. (1978)	Personal samples over 5 days	Spot samples (SG corrected = 1.021) for 5 days (midshift)	Ten individual means from heat sensor manufacturing (Figure 6)	1–7
Yamamura (1990)	Static samples over 4 days (TWA)	8-hr samples (corrected to unspecified SG) analyzed for inorganic mercury	Nine individual 8-hr composites of workers in thermometer plant B (Figure 5)	1–7

<sup>a</sup>Reported as total mercury in urine corrected to a specific gravity (SG) of 1.024 except as noted. <sup>b</sup>Figures and tables listed are from cited articles. <sup>c</sup>Converted from creatinine-corrected data to micrograms per liter; see "Methods."

urine samples separately for analysis from data on group means of several workers. The combined data set and the separate groups were analyzed using standard linear regression techniques and SYSTAT 9 statistical software (SPSS 1999). First, a regression model containing an interaction term was used to test for similarity of slopes among studies. When the interaction term was not significant, a simpler regression model without the slope interaction term was used to test for multiple intercept parameters. Additionally, the effect of different air-sampling methods used by the studies (i.e., personal air samplers on workers versus static area air samplers in the workplace) was examined.

**Results**

A total of 149 data points considered in the combined analysis from the various studies (Figure 2) yielded a significant correlation ( $R^2 = 0.599$ ;  $p < 0.001$ ;  $F = 219.5$ ;  $df =$

1,147) between mercury in air versus urine, including at lower air concentrations ranging from approximately 10 to 50  $\mu\text{g}/\text{m}^3$ . The regression equation model fit to all studies is

$$\log(\text{urine}) = \log(3.24) + 0.833 \times \log(\text{air})$$

or

$$\text{Urine} = 3.24 \times \text{air}^{0.833}.$$

The interaction term for separate slopes was not statistically significant, indicating similarity in slope among studies in the combined analysis ( $p = 0.512$ ). No obvious change in the shape of the relationship is apparent between airborne mercury levels above or below 50  $\mu\text{g}/\text{m}^3$ . However, because of significant differences in intercepts among studies, the more appropriate regression is a series of parallel lines with the same slope but different intercepts ( $b$ ) for each study ( $R^2 = 0.807$ ; Figure 3):

$$\text{Urine} = b \times \text{air}^{0.653}.$$

The studies appear to fall into two major groups (Table 5): one with intercept terms around 4–5, the other with higher intercepts around 6–13. At 50  $\mu\text{g}/\text{m}^3$ , the ratio between air and urine for the first group is about 1:1 to 1:1.5, whereas the ratio for the second group is 1:2 to 1:3. The difference between groups appears to be in large part due to the type of air-sampling methods used by the studies. For example, in the first group of studies, all but Mattiussi et al. (1982) used personal air samplers. Mattiussi et al. (1982), however, report that their results using either type of samplers were similar. In the second group, all but Stopford et al. (1978) used static area air samplers.

To evaluate whether predicted urinary levels at low airborne concentrations can be distinguished from background urinary mercury levels, urinary mercury predictions were examined near and below the lower limit of the data for the various log-log regression equations (Table 5). At an airborne mercury level of 10  $\mu\text{g}/\text{m}^3$ , the lower urinary predictions (based primarily on personal air sampling data) are similar to the upper bound background level of 20  $\mu\text{g}/\text{L}$ ,

**Table 3.** Summary of air and urine mercury data for studies included in analysis.

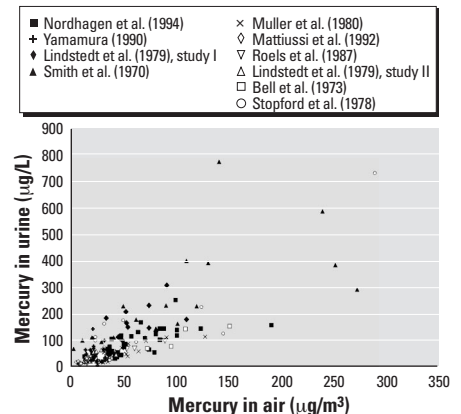
Study	n	Air ( $\mu\text{g}/\text{m}^3$ )			Urine ( $\mu\text{g}/\text{L}$ )		
		Min	Max	Mean	Min	Max	Mean
Bell et al. (1973)	4	73.1	151	107	70.0	154	112
Lindstedt et al. (1979), study I	13	34.3	111	63.3	76.0	307	162
Lindstedt et al. (1979), study II	15	14.7	43.0	23.0	23.4	65.4	39.1
Mattiussi et al. (1982)	21	6.1	37.8	16.7	10.8	50.4	25.6
Muller et al. (1980)	15	28.7	128	54.5	17.8	115	58.0
Nordhagen et al. (1994)	34	13.4	191	61.9	31.0	251	92.3
Roels et al. (1987)	10	15.7	89	40.9	13.4	100	51.5
Smith et al. (1970)	18	3.5	272	102	68.2	773	255
Stopford et al. (1978)	10	24.0	289	82.0	27.4	730	183
Yamamura et al. (1990)	9	14.0	22.0	19.3	25.0	145	71.1

**Table 4.** Comparison of regression statistics reported by previous studies to current study attempt to duplicate these results.<sup>a</sup>

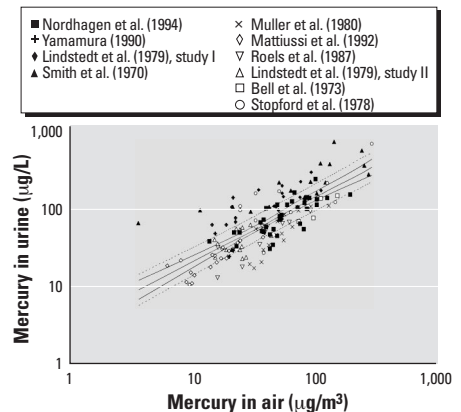
Study	Correlation	Fitted line	
		Intercept	Slope
Ehrenberg et al. (1991) <sup>b</sup>			
Reported	0.88	6.71	1.21
Current study	0.88	8.77	1.24
Lindstedt et al. (1979), study I <sup>c,d</sup>			
Reported	0.64	34.62	1.91
Current study	0.46	77.1	1.33
Lindstedt et al. (1979), study II <sup>c,d</sup>			
Reported	0.34	4.6	0.14
Current study	0.34	22.9	0.70
Mattiussi et al. (1982) <sup>d</sup>			
Reported	NR	5.82	1.18
Current study	0.91	5.83	1.18
Nordhagen et al. (1994)			
Reported	0.70	32.00	1.00
Current study	0.69	32.01	0.97
Roels et al. (1987)			
Reported	0.81	10.20	1.01
Current study	0.82	9.75	1.00
Stopford et al. (1978)			
Reported	0.88	NR	NR
Current study	0.90	7.57	2.13

NR, not reported.

<sup>a</sup>Current study analysis presented here conducted on data as reported by individual study. Air and urine data were scanned from figures presented in previous studies except as noted. <sup>b</sup>This study did not meet the criteria for inclusion in full analysis. <sup>c</sup>Urine data converted from nanomole per liter to microgram per liter to  $\mu\text{g}/\text{L}$ . <sup>d</sup>Individual data points reported by study.



**Figure 1.** Untransformed data used in current study.



**Figure 2.** Log-transformed data used in current study. Solid lines indicate fitted regression line with 95% confidence interval. Dashed lines indicate 95% prediction interval.

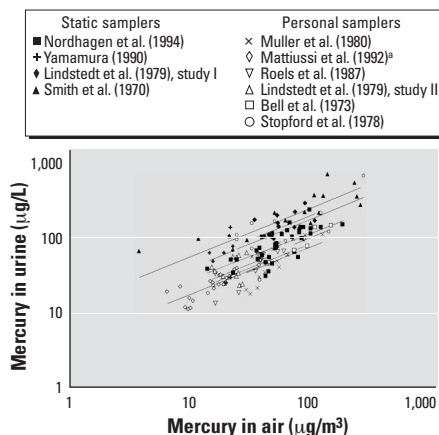


whereas the higher predictions (based primarily on static air sampling data) are above the background range. Assuming that this same relationship can be extrapolated below the available data to  $1 \mu\text{g}/\text{m}^3$ , the predicted urinary mercury levels for the lower range group is  $4\text{--}5 \mu\text{g}/\text{m}^3$  (similar to the mean reported background level).

A separate analysis of the seven studies reporting mean urine data for individual workers likewise showed a common slope term (slope interaction term was not significant; slope = 0.802;  $p = 0.487$ ) but different intercept terms for each study ( $p < 0.0001$ ; Table 6).

A simpler model was used to examine whether the intercepts for each study could be accounted for by the air sampling method (i.e., personal versus static). Although the model was significant (i.e., intercepts were higher for static area samplers than for personal air monitors;  $p < 0.001$ ;  $F = 56.7$ ;  $df = 2,73$ ), it was not significantly better than with individual study intercepts (adjusted  $R^2$  of 0.597 vs. 0.687). Only two studies used static rather than personal sampling methods in this individual mean group (Lindstedt et al. 1979 [study I]; Yamamura 1990). Unlike the other studies (except Lindstedt et al. 1979 [study II]), a significant relationship between air and urine mercury concentration was not found for these two studies.

The three studies reporting urine data based on group means of workers also showed a similar slope among studies (non-significant interaction term,  $F = 2.40$ ;  $p = 0.098$ ;  $df = 2,67$ ) with different intercept terms ( $F = 44.99$ ;  $p < 0.0001$ ;  $df = 2,69$ ; Table 7), although the slope (0.592) was lower and the intercept terms higher than for the seven studies reporting individual mean data. All three studies in this group used static air samplers.



**Figure 3.** All data used in current study with separate fitted lines.

<sup>a</sup>Static sampler results were equivalent to personal sampler results.

## Discussion

**Relationship between mercury in air and in urine.** A significant correlation was found between mercury in air and in urine that extends  $< 50 \mu\text{g}/\text{m}^3$ , although data were not available for values  $< 3 \mu\text{g}/\text{m}^3$ . Nevertheless, no change in slope was observed through the range of data. The slope of the relationship was also less affected than the intercept by differences among studies in the type of air-sampling methods (i.e., personal air monitors vs. static area air samplers) or how urinary data were grouped (i.e., individual mean vs. group mean). Consequently, the relationships derived from this pooled analysis of studies appear useful for assessing the effects of low airborne mercury levels on urinary mercury levels. The lower intercept terms, based largely on personal sampling data, appear to be the more accurate predictor of urinary mercury levels associated with a given air mercury level.

Although urinary mercury levels can be related to airborne mercury levels down to about  $10 \mu\text{g}/\text{m}^3$  with some confidence, extrapolations to lower concentrations such as  $1 \mu\text{g}/\text{m}^3$  are uncertain and likely inaccurate. Specifically, at  $1 \mu\text{g}/\text{m}^3$ , the log-log or exponential regression equation predicts an airborne mercury contribution to urine of  $1 \mu\text{g}/\text{L}$  and a total predicted urinary level that is equivalent to the intercept term (i.e.,  $4\text{--}5 \mu\text{g}/\text{L}$ ). This intercept term in part reflects an average of background sources of mercury in urine for the workers in the studies. Extrapolations below the lower end of the data, however, should be interpreted with caution because any inaccuracies in the slope have a greater impact at the high and low ends of the air concentration range. In reality, the observed decrease in urinary mercury levels with decreasing air mercury levels would likely end  $< 10 \mu\text{g}/\text{m}^3$  as background sources

**Table 5.** Regression results and predicted urinary mercury concentrations (microgram per liter) at various airborne mercury concentrations for all studies combined.

Study	1 $\mu\text{g}/\text{m}^3$	10 $\mu\text{g}/\text{m}^3$	50 $\mu\text{g}/\text{m}^3$
Muller et al. (1980) <sup>a</sup>	3.8	17	49
Mattiussi et al. (1982) <sup>b</sup>	4.0	18	51
Roels et al. (1987) <sup>a</sup>	4.3	19	55
Lindstedt et al. (1979), study II <sup>a</sup>	4.9	22	63
Bell et al. (1973) <sup>a</sup>	5.1	23	66
Nordhagen et al. (1994) <sup>c</sup>	6.0	27	77
Yamamura (1990) <sup>c</sup>	9.1	41	117
Stopford et al. (1978) <sup>a</sup>	9.2	41	118
Lindstedt et al. (1979), study I <sup>c</sup>	10.4	47	134
Smith et al. (1970) <sup>c</sup>	13.1	59	168

95% confidence interval on slope (0.543, 0.763);  $p < 0.001$ ;  $f = 57.6$ ;  $df = 10,138$ . Urine =  $b \times \text{air}^{0.653}$ , where  $b$  = predicted urinary concentration at  $1 \mu\text{g}/\text{m}^3$ . <sup>a</sup>Used personal air samplers. <sup>b</sup>Used static air samplers but reported that results are similar to personal air samplers. <sup>c</sup>Used static air samplers.

of mercury in the urine begin to dominate. Based on data primarily from more accurate personal air samplers (data sets with intercepts of  $4\text{--}5$  in Table 5), at  $10 \mu\text{g}/\text{m}^3$  the predicted urinary mercury concentrations are at the upper bound of background ( $20 \mu\text{g}/\text{L}$ ; Table 1), whereas below this level in the  $1\text{--}5 \mu\text{g}/\text{m}^3$  range, the extrapolated urinary mercury levels are well within background levels (i.e., near the mean of  $4\text{--}5 \mu\text{g}/\text{L}$ ; Table 1; Figure 4).

Two other studies that lacked sufficient detail to include in the current analysis also indicate that the background concentrations in the urine would limit the relationship between mercury in air and urine. Ishihara et al. (1977) reported that the mean urinary mercury level of 14 female workers ( $2.64 \mu\text{g}/\text{L}$ ) did not change after 4 months or 8 months of exposure to mercury vapor in the range of  $1\text{--}19 \mu\text{g}/\text{m}^3$ . Likewise, Cianciola et al. (1997) reported that low levels of mercury in air were not significantly correlated with urine mercury levels for 69 dental professionals. Specifically, geometric mean air levels of 6.5, 3.1, and  $1.4 \mu\text{g}/\text{m}^3$  for three job categories corresponded to urinary mercury levels of 3.1, 3.9, and  $2.0 \mu\text{g}/\text{L}$ , respectively.

The implication of these findings is that urinary mercury is not a useful quantitative measure of mercury exposure at low air concentrations  $< 10 \mu\text{g}/\text{m}^3$  even though public health guidelines (i.e., the  $1 \mu\text{g}/\text{m}^3$  ATSDR residential action level) may be exceeded.

**Comparison to other studies.** Comparison to previous studies is complicated by the lack

**Table 6.** Regression results and predicted urinary mercury concentrations (micrograms per liter) at various airborne mercury concentrations for individual mean urine data.

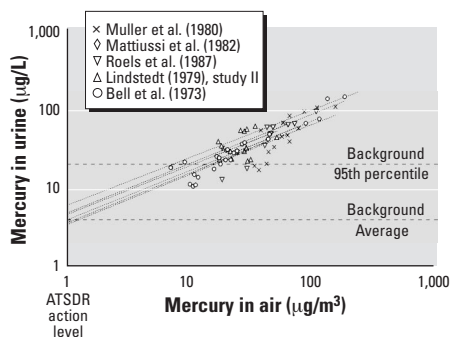
Study	1 $\mu\text{g}/\text{m}^3$	10 $\mu\text{g}/\text{m}^3$	50 $\mu\text{g}/\text{m}^3$
Muller et al. (1980) <sup>a</sup>	2.1	14	49
Roels et al. (1987) <sup>a</sup>	2.5	16	58
Bell et al. (1973) <sup>a</sup>	2.6	16	59
Lindstedt et al. (1979), study II <sup>a</sup>	3.1	19	71
Yamamura (1990) <sup>b</sup>	3.5	22	82
Stopford et al. (1978) <sup>a</sup>	5.0	32	116
Lindstedt et al. (1979), study I <sup>b</sup>	5.7	36	130

95% confidence interval on slope (0.577, 1.027);  $p < 0.001$ ;  $f = 24.5$ ;  $df = 7,68$ . Urine =  $b \times \text{air}^{0.802}$ , where  $b$  = predicted urinary concentration at  $1 \mu\text{g}/\text{m}^3$ . <sup>a</sup>Used personal air samplers. <sup>b</sup>Used static air samplers.

**Table 7.** Regression results and predicted urinary mercury concentrations ( $\mu\text{g}/\text{L}$ ) at various airborne mercury concentrations for group mean urine data.

Study	1 $\mu\text{g}/\text{m}^3$	10 $\mu\text{g}/\text{m}^3$	50 $\mu\text{g}/\text{m}^3$
Mattiussi et al. (1982)	4.7	18	48
Nordhagen et al. (1994)	7.6	30	77
Smith et al. (1970)	8.5	33	86

95% confidence interval on slope (0.474, 0.710);  $p < 0.001$ ;  $f = 156.8$ ;  $df = 3,69$ ; all studies used static air samplers.



**Figure 4.** Comparison of predicted urinary mercury levels at low airborne levels to background urinary mercury levels.

of log transformation of the data in these studies, even though such a transformation provides better adherence to model distribution and variability assumptions. Thus, the slope in our predicted regression equations cannot be directly interpreted as the simple linear contribution to mercury urine levels by a change in air concentration. In a log-log relationship, the predicted amount of increase in the urine level changes as an exponential function of the air concentration multiplied by an intercept term. The potential effect of mercury in air on mercury levels in urine predicted by this exponential function should be recognized as including background sources of exposure in the worker populations studied and other factors such as the air-sampling methodology.

At 50  $\mu\text{g}/\text{m}^3$ , our predicted relationship for mercury in air and urine is consistent with discussion of this ratio in the occupational literature (e.g., 1:1 to 1:3) (Bell et al. 1973; Lauwerys and Buchet 1973; Mattiussi et al. 1982; Muller et al. 1980; Roels et al. 1987; Schuckmann 1979). As noted above, differences in these ratios appear to be due to the type of air-sampling devices used in the individual studies. Comparisons of this predicted ratio at lower air concentrations with the literature cannot be made because the ratio between air and urine mercury varies as a function of the regression equation and is not constant with air mercury concentration (Mattiussi et al. 1982).

**Averaging of urinary data and air sampling methodology.** Because of differences between urine sample types (i.e., individual mean vs. group mean), separate rather than combined regression analysis of these groups is warranted. Whether the individual mean or group mean data analysis is more representative of the relationship between air and urine mercury levels, however, is complicated by the small number of group mean studies, all of which used static area air samplers.

Our findings also indicate that static air samplers underestimate airborne mercury exposure to workers (Sällsten et al. 1992),

thereby inflating predictions of urinary mercury at a given air concentration. In the combined analysis of all studies, four of the five highest intercept terms (and therefore urinary predictions) were from studies using static samples (Lindstedt et al. 1979 [study I]; Nordhagen et al. 1994; Smith et al. 1970; Yamamura 1990). In the individual mean urinary data analysis, the intercept term was significantly lower for personal versus static samples. The nonsignificant regression for the static air sampler studies in this analysis (Lindstedt et al. 1979 [study I]; Yamamura 1990) may be indicative of static air samples being less correlated with worker exposure and therefore urinary measurements. In addition, two of the three studies reporting group mean urine data (all used static air samplers) showed much higher intercept terms (Table 7) than the studies reporting individual mean data (which included mostly personal samplers). The one study (Mattiussi et al. 1982) in this group of three with a relatively low intercept term (4.7) reported that their results were similar for either personal or static sampling equipment.

**Other sources of variation in urinary mercury levels.** Other factors that might affect observed relationships between air and urine mercury levels include how well studies controlled for intra- and interindividual variation in urine mercury and differences in background levels among worker populations. Uncertainties in measurements include analytical methods and correction for hydration state: creatinine correction by Roels et al. (1987), no correction by study I of Lindstedt et al. (1979); and possibly Nordhagen et al. (1994), and correction to different specific gravity levels by Muller et al. (1980) and Stopford et al. (1978). Uncorrected data have within-individual variation due to the hydration state of the urine sample, although correction based on creatinine content introduces some uncertainty due to variation in creatinine excretion with time of day, gender, diet, etc. (Boeniger et al. 1993). Correction to different specific gravity levels and differences in background urinary mercury levels likely affect the intercept term of studies more than the slope of the air versus urine relationship. Potential variation among studies is in part ameliorated by our selection of studies that used standardized methods to collect urine (e.g., sampling at a specific time of the day) and averaged multiple samples within or among individuals.

**Application to the general population.** Variation in background exposures to mercury complicates these studies of low-level exposure in workers and application to the general population. In addition, the studies

evaluated span a number of years over which the quality of the laboratory data varied and included several different countries where exposures may vary. A common source of elemental mercury exposure for most people is dental amalgams, and the number of dental amalgams may account for much of the interindividual differences in background levels of mercury in urine (ATSDR 1999). Jokstad et al. (1992) reported that persons with 36–69 amalgam-restored surfaces were estimated to have a mean mercury urine concentration of 6  $\mu\text{g}/\text{L}$  compared to 1.2  $\mu\text{g}/\text{L}$  in those without amalgams. Sandborgh-Englund et al. (1998) found that urine mercury levels after removal of dental amalgams decreased to approximately 60% of pre-removal levels. Background mercury exposure in the general population resulting from dental amalgams, however, is generally not considered harmful [ATSDR 1999; U.S. Public Health Service (U.S. PHS) 1993; Clarkson 2002], although Echeveria et al. (1998) reported subtle neurobehavioral effects in dental personnel.

With the decrease in the use of mercury-containing dental amalgams and other products in the United States, background levels of mercury in the urine are likely decreasing toward the 1.2  $\mu\text{g}/\text{L}$  level reported by Jokstad et al. (1992). Background urinary mercury levels in children also appear to be lower than in adults (Table 1). A lower background urinary mercury level is expected to change the predicted relationship between mercury in air and urine by decreasing the intercept term rather than by changing the slope. Data were inadequate, however, to evaluate this relationship specifically for children. The intercept terms of our analysis reflect average background urinary mercury levels of worker populations in studies dating from the 1950s to the 1980s during which exposure to dental amalgams and other sources (e.g., latex paint) was more common. Industrial hygiene practices in the past also allowed some transport of mercury on workers' clothing and shoes to homes (Hudson et al. 1987).

Based on the relationship found in this study, a decrease in intercept term due to lower background urinary levels indicates that the actual contribution of mercury in air to mercury in urine at the low regulatory levels may still be indistinguishable from background levels even in the future.

## Conclusion

A correlation between air and urine mercury does exist at airborne mercury levels < 50  $\mu\text{g}/\text{m}^3$ . However, the relationship between urinary mercury and airborne concentrations of elemental mercury is only reliable down to concentrations of about 10  $\mu\text{g}/\text{m}^3$ . Below 10

$\mu\text{g}/\text{m}^3$ , predicted urinary mercury levels are within background ranges. Urinary mercury is therefore not an accurate measure for understanding the exposure of persons due to most environmental air concentrations, which are typically well below  $10 \mu\text{g}/\text{m}^3$ . The effect of an air concentration at the ATSDR residential action level of  $1 \mu\text{g}/\text{m}^3$  on the urinary mercury level appears negligible relative to background levels.

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