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Estimation of Dietary Pb and Cd Intake from Pb and Cd in Blood or Urine

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Abstract Successful trials were made to estimate the dietary daily intake of lead (Pb) and cadmium (Cd) via foods from the levels of the metals in blood or urine. In practice, 14 and 15 reports were available for Pb and Cd in blood (Pb-B and Cd-B), urine (Pb-U and Cd-U) and 24-h diet duplicates (Pb-D and Cd-D), respectively, from which 68 pairs each of Pb or Cd in blood and food duplicates [each being geometric mean (GM) values for the survey sites] were obtained. Regression analysis revealed that there was a significant correlation between Pb-B and Pb-D, and also between Cd-B and Cd-D, suggesting that it should be possible to estimate both Pb-D and Cd-D from Pb-B and Cd-B, respectively. For Cd-U, the number of available cases was limited (20 pairs), but a significant correlation was detected between Cd-U (as Cd-U$_{cr}$, or Cd levels in urine as corrected for creatinine concentration) and Cd-D. Care should be taken in estimating Pb-D from Pb-B, as the ratio of Pb-D over Pb-B may decrease as a function of increasing Pb-B levels. The Pb-D (μg/day) for typical Japanese women with Pb-B of 15 μg/l was best estimated to be 13.5 μg/day. No Cd-B- or Cd-U$_{cr}$-dependent change was detected in case of Cd. The best estimate of Cd-D for Cd-B at 1.5 μg/l should be about 19.4 μg/day.

Keywords Blood · Cadmium · Daily diet · Lead · Urine

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Introduction

Dietary intake of ubiquitous heavy metals such as cadmium (Cd) and lead (Pb) are among the foci of public concern especially as the metal levels in atmosphere has been gradually decreasing in many countries including Japan, so that body burden via respiratory route will be less important whereas metal intake via foods remains as the major source [1–3]. Although it is desirable to have data on dietary metal intake, such procedures as 24-h food duplicate collection followed by instrumental analyses for metals to obtain reliable estimate for dietary intake are not only complex but time- and hand-consuming [4–6].

In the present analysis, data were collected from previous publications on Cd and Pb in blood, urine and diet (Cd-B, Pb-B, Cd-U, Pb-U, Cd-D and Pb-D, respectively) of populations mostly in Japan and in east or south-east Asia, and correlations among the parameters were examined for a possibility that Pb-D and Cd-D may be estimated from Pb-B and Cd-B, respectively, or Cd-D from Cd-U.

Materials and Methods

Data from Literature

Data are all on general populations without occupational exposure to Pb or Cd, and cited from previous publications, i.e. references [7–19, 22, 45] for Pb in blood, urine or 24-h food duplicate samples, and references [7–16, 18, 20–23, 45] for Cd in blood, urine or 24-h food duplicate samples (Tables 1 and 2). Regarding Cd-U, the values as corrected for creatinine (Cd-U_{cr}) [24] rather than non-corrected values (CdU_{ob}) were employed simply because the published data were more abundant for Cd-U_{cr} than Cd-U_{ob} despite the criticism that creatinine correction may induce biases especially among aged people [25].

Watanabe et al. [12] published GM values for Cd-B, Cd-D, Pb-B and Pb-D in 38 sites, i. e. 19 sites being studied twice, 10 years apart. From the 38 data sets, those with ≧10 pairs of data on blood and food duplicates were selected so that 32 sets were taken for present analysis.

Using the market basket method [4], Matsuda [18] reported on dietary Cd and Pb intake for adult Japanese (assumedly at the ages of 40–59 years, men and women not specified). In the report, Cd and Pb intakes were given by food groups, e.g. cereals, animal meats, fish and shellfish etc. similar to the classification by Ministry of Health, Labour and Welfare, Japan [26]. The report [26] describes per capita per day food consumption (in weight) among Japanese populations by age groups (1–6, 7–14, 15–19 and 20–29 years, and by decade up to 69, and ≧70 years of age) and for men and women combined and also separately. It is known that adult men take more cereals (typically rice, the leading source of dietary Cd in Japan [13]) than adult women [26]. Thus, Cd intake for adult women for example was estimated for each food group assuming that the Cd intake for women was proportional to the amount (in weight) of food consumed [i.e. Cd in the food group × (food amount for women/food amount for men and women combined)], which was followed by summation for all food groups to estimate daily intake via foods. The same assumption of Cd (or Pb) intake proportional to the amount of foods in the food groups was taken in cases of estimation for dietary Cd or Pb intake of children except that boys and girls were treated as combined.

Table 1 The database for Pb internal dose and dietary intake

Reference	Country/Area	Location	Gender, etc.	Year of study	Pb-B			$Pb\text{-}U_{cr}$			Pb-D			Pb-B over Pb-D	Pb-Ucr over Pb-D
					GM (μg/l)	GSD	*N*	GM (μg/l)	GSD	*N*	GM (μg/l)	GSD	*N*		
Ref. [7]	Korea	Busan	Children[b]	2000	38.0	1.57	38	6.92	1.59	38	8.2	2.36	38	4.63	0.843
Ibid.	Korea	Busan	Mothers[c]	2000	37.3	1.70	38	5.13	2.28	38	18.4	1.78	38	2.03	0.279
Ref. [8]	Korea	Seoul	Women	1994	46.6	1.21	24				17.5	1.68	24	2.66	
Ibid.	Korea	Chunan	Women	1994	59.9	1.34	29				21.7	1.53	29	2.76	
Ibid.	Korea	Haman	Women	1994	33.4	1.33	41				20.2	1.70	41	1.65	
Ibid.	Korea	Pusan	Women	1994	46.0	1.33	47				21.6	1.67	47	2.13	
Ref. [9]	Malaysia	Kuala Lumpur	Women	1995	45.6	1.35	49				10.1	1.88	52	4.51	
Ref. [10]	Taiwan	Tainan	Women	1994	44.5	1.28	52				22.4	1.93	52	1.99	
Ref. [11]	Japan	All Japan	Women	2003–2008	15.5[i]	1.51	1227				20.1[i]			0.77	
Ibid.	Japan	Hirosaki city	Women	2008	13.8[i]	1.60	100				20.1[i]			0.69	
Ibid.	Japan	Fukui city	Women	2008	14.2[i]	1.44	106				20.1[i]			0.71	
Ref. [12]	Japan	Abuta	Women	1980	33.6	1.33	56				38.5	1.68	17	0.87	
Ibid.	Japan	Nankodai	Women	1980	52.3	1.53	20				22.0	1.83	20	2.38	
Ibid.	Japan	Akiu	Women	1980	35.0	1.35	19				25.3	1.42	15	1.38	
Ibid.	Japan	Shironé	Women	1980	32.7	1.51	19				40.7	2.09	18	0.80	
Ibid.	Japan	Toyama	Women	1980	31.9	1.39	23				56.7	1.7	16	0.56	
Ibid.	Japan	Fukagawa	Women	1980	61.6	1.44	22				55.2	1.65	24	1.12	
Ibid.	Japan	Kanazawa	Women	1980	33.1	1.39	20				41.8	1.72	19	0.79	
Ibid.	Japan	Hikawa	Women	1980	21.6	1.47	27				31.5	1.46	20	0.69	
Ibid.	Japan	Geisei	Women	1980	21.0	1.53	16				42.5	2.01	17	0.49	
Ibid.	Japan	Tsuyazaki	Women	1980	26.2	1.40	26				31.7	1.42	26	0.83	
Ibid.	Japan	Amami	Women	1980	30.7	1.37	52				25.9	1.67	21	1.19	
Ibid.	Japan	Fukiagé	Women	1980	27.6	1.57	31				23.1	1.58	26	1.19	
Ibid.	Japan	Aira	Women	1980	42.5	1.35	25				21.7	2.32	19	1.96	
Ibid.	Japan	Misato	Women	1980	45.1	1.51	21				28.5	1.59	11	1.58	
Ibid.	Japan	Miyako	Women	1980	27.8	1.47	38				17.2	1.36	10	1.62	

Table 1 (continued)

Reference	Country/Area	Location	Gender, etc.	Year of study	Pb-B			Pb-U$_{cr}$			Pb-D			Pb-B over Pb-D	Pb-Ucr over Pb-D
					GM (μg/l)	GSD	*N*	GM (μg/l)	GSD	*N*	GM (μg/l)	GSD	*N*		
Ibid.	Japan	Abuta	Women	1990	21.2	1.33	37				4.0	2.85	32	5.30	
Ibid.	Japan	Nankodai	Women	1990	26.2	1.50	19				9.1	1.66	19	2.88	
Ibid.	Japan	Kanan	Women	1990	30.5	1.37	18				8.7	1.54	10	3.51	
Ibid.	Japan	Akiu	Women	1990	22.8	1.52	18				4.0	2.35	15	5.70	
Ibid.	Japan	Kitakata	Women	1990	12.2	1.92	28				14.5	2.09	29	0.84	
Ibid.	Japan	Shironé	Women	1990	24.5	1.37	24				2.2	2.68	22	11.14	
Ibid.	Japan	Toyama	Women	1990	25.2	1.48	26				6.0	3.02	25	4.20	
Ibid.	Japan	Fukagawa	Women	1990	37.8	1.47	21				6.8	3.28	23	5.56	
Ibid.	Japan	Kanazawa	Women	1990	22.0	1.51	24				7.8	2.56	24	2.82	
Ibid.	Japan	Hikawa	Women	1990	25.8	1.46	33				7.8	2.96	28	3.31	
Ibid.	Japan	Geisei	Women	1990	19.9	1.30	20				4.2	2.07	17	4.74	
Ibid.	Japan	Tsuyazaki	Women	1990	17.4	1.32	16				6.6	1.85	14	2.64	
Ibid.	Japan	Amami	Women	1990	15.2	1.91	22				11.7	2.39	23	1.30	
Ibid.	Japan	Fukiagé	Women	1990	25.0	1.60	29				10.6	2.16	28	2.36	
Ibid.	Japan	Aira	Women	1990	27.8	1.39	28				10.1	2.38	28	2.75	
Ibid.	Japan	Misato	Women	1990	32.7	1.45	29				10.2	2.23	10	3.21	
Ibid.	Japan	Miyako	Women	1990	21.3	1.37	52				7.5	3.15	22	2.84	
Ref. [13]	China	Xian	Women	1997	43.4	1.32	50	7.03	2.49	50	26.1	1.64	50	1.66	0.269
Ibid.	China	Gongzhang	Women	1997	38.2	1.46	49	4.29	1.96	49	28.1	1.48	49	1.36	0.153
Ibid.	China	Baoji	Women	1997	21.5	1.37	50	4.03	1.89	50	36.0	1.49	50	0.60	0.112
Ref. [14]	China	Beijing	Women	1993–1995	53.2	1.41	50				31.8	3.12	24	1.67	
Ibid.	China	Shanghai	Women	1993–1995	79.0	1.50	50				17.0	1.72	50	4.65	
Ibid.	China	Nannin	Women	1993–1995	56.0	1.47	50				37.3	1.99	50	1.50	
Ibid.	China	Tainan	Women	1993–1995	44.5	1.28	52				22.2	1.95	48	2.00	
Ibid.	Japan	Tokyo	Women	1993–1995	30.6	1.62	39				9.3	4.39	39	3.29	

Ibid.	Japan	Kyoto	Women	1993–1995	45.6	2.05	17				14.6	3.6	17	3.12	
Ibid.	Japan	Sendai	Women	1993–1995	25.3	1.48	16				15.6	1.75	16	1.62	
Ref. [15]	The Philippines	Manila	Women	1997	37	1.36	45				11.1	1.74	45	3.33	
Ref. [16]	Korea	Seoul etc.	Adults	1999–2000	28.9		30				16.4		30	1.76	
Ref. [17][a]	Japan	Shizuoka pref.	Children[d]		17.1	1.11	20				13.1[j]			1.30	
Ibid.	Japan	Shizuoka pref.	Children[e]		13.0	1.09	60				13.1[j]			0.99	
Ibid.	Japan	Shizuoka pref.	Children[f]		14.1	1.09	36				18.8[j]			0.75	
Ibid.	Japan	Shizuoka pref.	Children[g]		12.1	1.08	61				18.8[j]			0.64	
Ref. [19][a]	Japan	Unknown	Children[h]		11.8[i]	1.1	132				16.5[j]			0.72	
Ref. [22]	Thailand	Bangkok	Women	1998	30.7	1.38	36	2.00	1.51	36	14.1	1.76	36	2.18	0.142
Ref. [45]	Japan	Hokkaido	Women	1991–1998	17.1	1.87	51	5.15	1.98	51	4.90	3.44	51	3.49	1.051
Ibid.	Japan	Tohoku	Women	1991–1998	18.9	1.74	145	1.23	2.76	145	8.34	2.53	145	2.27	0.147
Ibid.	Japan	Kanto-Tokai	Women	1991–1998	16.9	2.18	123	1.70	2.70	123	7.79	2.09	123	2.17	0.218
Ibid.	Japan	Hokuriku	Women	1991–1998	20.7	1.94	75	3.55	2.48	75	8.52	2.68	75	2.43	0.417
Ibid.	Japan	Kinki	Women	1991–1998	21.5	1.99	83	2.01	3.37	83	8.47	2.40	83	2.54	0.237
Ibid.	Japan	Chu-Shikoku	Women	1991–1998	18.8	1.90	63	2.73	3.55	63	9.36	2.27	63	2.01	0.292
Ibid.	Japan	Kyushu-Okinawa	Women	1991–1998	20.9	1.44	67	1.94	2.72	67	5.62	2.18	67	3.72	0.345

Pb-B, Pb-Ucr and Pb-D stand for Pb in blood, in urine as corrected for creatinine and in 24-h food duplicate, respectively, unless otherwise specified. Analyses were by graphite furnace atomic absorption spectrometry, unless otherwise specified. GM, GSD and N stand for geometric mean, geometric standard deviation and numbers of case, respectively

[a] The moment method [28] was applied to estimate GM and GSD from AM and ASD

[b] 4–10-year-olds, boys and girls mixed

[c] 28-46 yr-olds

[d] 1–5-yr-olds from smoking families

[e] 1–5 year-olds from non-smoking families

[f] 6–14-year-olds from smoking families

[g] 6–14-year-olds from non-smoking families

[h] 1–15-year-olds

[i] By inductively-coupled plasma-mass spectrometry

[j] Estimated frrom market basket-based data of Matsuda [18]; see the "Materials and Methods" section for details of estimation procedures

Table 2 The database for Cd internal dose and dietary intake

Reference	Country/Area	Location	Gender, etc.	Year of study	Cd-B			$Cd\text{-}U_{cr}$			Cd-D			Cd-B over Cd-D	Cd-Ucr over Cd-D
					GM (μg/l)	GSD	N	GM (μg/l)	GSD	N	GM (μg/l)	GSD	N		
Ref. [7]	Korea	Busan	Children[a]	2000	1.51	1.67	38	1.69	1.60	38	11.2	2.00	38	0.135	0.151
Ibid.	Korea	Busan	Mothers[b]	2000	2.74	1.75	38	1.56	1.73	38	16.7	1.84	38	0.164	0.093
Ref. [8]	Korea	Seoul	Women	1994	1.21	1.49	24				14.3	1.71	24	0.085	
Ibid.	Korea	Chunan	Women	1994	1.03	1.78	29				19.6	1.61	29	0.053	
Ibid.	Korea	Haman	Women	1994	1.55	1.51	41				24.2	1.82	41	0.064	
Ibid.	Korea	Pusan	Women	1994	1.25	1.77	47				24.3	1.54	47	0.051	
Ref. [9]	Malaysia	Kuala Lumpur	Women	1995	0.71	2.02	49				7.31	2.58	49	0.097	
Ref. [10]	Taiwan	Tainan	Women	1994	1.11	1.39	52				10.1	1.70	52	0.110	
Ref. [11]	Japan	All Japan	Women	2003-8	1.23[c]	1.70	1227				20.6[d]			0.060	
Ibid.	Japan	Hirosaki city	Women	2008	1.37[c]	1.66	100	1.01	1.88	100	20.6[d]			0.066	0.049
Ibid.	Japan	Fukui city	Women	2008	1.38[c]	1.67	106	0.64	2.30	106	20.6[d]			0.067	0.031
Ref. [12]	Japan	Abuta	Women	1980	3.89	1.33	56				35.3	1.69	17	0.110	
Ibid.	Japan	Nankodai	Women	1980	4.08	1.21	20				29.5	1.65	20	0.138	
Ibid.	Japan	Akiu	Women	1980	3.15	1.38	19				26.7	1.86	15	0.118	
Ibid.	Japan	Shironé	Women	1980	3.84	1.26	19				71.4	1.57	18	0.054	
Ibid.	Japan	Toyama	Women	1980	4.81	1.6	23				63.7	1.38	16	0.076	
Ibid.	Japan	Fukagawa	Women	1980	3.68	1.29	22				27.6	1.53	24	0.133	
Ibid.	Japan	Kanazawa	Women	1980	3.16	1.48	20				50.5	1.55	19	0.063	
Ibid.	Japan	Hikawa	Women	1980	4.84	1.29	27				86.8	1.39	20	0.056	
Ibid.	Japan	Geisei	Women	1980	3.05	1.27	16				33.3	1.59	17	0.092	
Ibid.	Japan	Tsuyazaki	Women	1980	3.94	1.47	26				92.3	1.69	26	0.043	
Ibid.	Japan	Amami	Women	1980	2.92	1.47	52				19.5	1.31	21	0.150	
Ibid.	Japan	Fukiagé	Women	1980	2.64	1.34	31				23.5	1.62	26	0.112	
Ibid.	Japan	Aira	Women	1980	2.01	1.38	25				23.2	1.25	19	0.087	
Ibid.	Japan	Misato	Women	1980	2.83	1.31	21				29.2	1.41	11	0.097	

Ibid.	Japan	Miyako	Women	1980	3.31	1.43	38				30.1	1.37	10	0.110	
Ibid.	Japan	Abuta	Women	1990	2.25	1.5	37				18.9	1.97	32	0.119	
Ibid.	Japan	Nankodai	Women	1990	2.11	1.74	19				22.8	1.87	19	0.093	
Ibid.	Japan	Kanan	Women	1990	1.99	1.32	18				29.0	1.53	10	0.069	
Ibid.	Japan	Akiu	Women	1990	2.66	1.45	18				16.9	1.48	15	0.157	
Ibid.	Japan	Kitakata	Women	1990	3.27	1.6	28				58.1	1.86	29	0.056	
Ibid.	Japan	Shironé	Women	1990	3.93	1.37	24				67.3	1.65	22	0.058	
Ibid.	Japan	Toyama	Women	1990	3.76	1.49	26				64.5	1.84	25	0.058	
Ibid.	Japan	Fukagawa	Women	1990	1.63	1.52	21				32.6	2.49	23	0.050	
Ibid.	Japan	Kanazawa	Women	1990	2.57	1.83	24				45.8	1.54	24	0.056	
Ibid.	Japan	Hikawa	Women	1990	2.41	1.5	33				41.6	1.74	28	0.058	
Ibid.	Japan	Geisei	Women	1990	1.73	1.49	20				20.1	1.55	17	0.086	
Ibid.	Japan	Tsuyazaki	Women	1990	2.50	1.54	16				32.9	1.5	14	0.076	
Ibid.	Japan	Amami	Women	1990	0.96	1.48	22				16.7	1.74	23	0.057	
Ref. [13]	China	Xian	Women	1997	0.45	1.51	50	3.00	1.72	50	5.83	1.41	50	0.077	0.515
Ibid.	China	Gongzhang	Women	1997	0.52	1.48	49	2.46	1.51	49	6.79	1.43	49	0.077	0.362
Ibid.	China	Baoji	Women	1997	0.42	1.72	50	3.06	1.63	50	5.64	1.49	50	0.074	0.543
Ref. [14]	China	Beijing	Women	1993-5	0.79	1.54	50				5.8	1.87	24	0.136	
Ibid.	China	Shanghai	Women	1993-5	1.18	1.40	50				6.1	2.01	50	0.193	
Ibid.	China	Nannin	Women	1993-5	1.25	1.45	50				25.0	2.05	50	0.050	
Ibid.	China	Tainan	Women	1993-5	1.11	1.39	52				10.1	1.73	48	0.110	
Ibid.	Japan	Tokyo	Women	1993-5	1.82	1.57	39				33.4	2.08	39	0.054	
Ibid.	Japan	Kyoto	Women	1993-5	1.99	1.45	17				37.0	1.55	37	0.054	
Ibid.	Japan	Sendai	Women	1993-5	2.08	1.84	16				24.8	1.88	16	0.084	
Ref. [15]	The Philippines	Manila	Women	1997	0.47	1.87	45				14.2	2.77	45	0.033	
Ref. [16]	Korea	Seoul etc.	Adults	1999-2000	1.30						12.61			0.103	
Ref. [20]	Japan	3 prefectures	Women	1980	3.57	1.42	141				27.7	1.75	65	0.129	
Ibid.	Japan	3 prefectures	Women	1990	1.84	1.67	165				23.8	1.73	85	0.077	
Ref. [21]	China	Jinan	Women	1996	0.48	1.44	50				6.43	1.98	50	0.075	

Table 2 (continued)

Reference	Country/Area	Location	Gender, etc.	Year of study	Cd-B			Cd-U$_{cr}$			Cd-D			Cd-B over Cd-D	Cd-Ucr over Cd-D
					GM (μg/l)	GSD	N	GM (μg/l)	GSD	N	GM (μg/l)	GSD	N		
Ibid.	China	Baiquan	Women	1996	0.29	1.50	50				5.93	1.50	50	0.049	
Ref. [22]	Thailand	Bangkok	Women	1998	0.40	1.52	36	1.47	1.48	36	7.37	1.91	36	0.054	0.199
Ref. [23]	Japan	Village A	Women	2000-1	2.00	1.58	202	2.63	1.74	202	6.99	2.56	202	0.286	0.376
Ibid.	Japan	Village B	Women	2000-1	1.91	1.73	202	3.47	1.7	202	19.14	2.30	202	0.100	0.181
Ibid.	Japan	Village C	Women	2000-1	2.56	1.52	203	3.16	1.71	203	17.65	2.88	203	0.145	0.179
Ibid.	Japan	Village D	Women	2000-1	1.65	2.35	204	3.16	1.77	204	38.91	2.18	204	0.042	0.081
Ibid.	Japan	Village E	Women	2000-1	3.61	1.63	569	4.08	1.74	569	51.99	2.25	569	0.069	0.078
Ref. [45]	Japan	Hokkaido	Women	1991-1998	2.17	1.52	51	5.69	1.39	51	18.7	1.88	51	0.12	0.30
Ibid.	Japan	Tohoku	Women	1991-1998	1.42	2.12	145	3.16	2.00	145	20.7	2.54	145	0.07	0.15
Ibid.	Japan	Kanto-Tokai	Women	1991-1998	1.80	1.51	123	3.42	1.67	123	23.0	2.12	123	0.08	0.15
Ibid.	Japan	Hokuriku	Women	1991-1998	3.74	1.50	75	7.78	2.18	75	53.2	1.72	75	0.07	0.15
Ibid.	Japan	Kinki	Women	1991-1998	1.02	2.26	83	2.40	2.38	83	23.4	2.13	83	0.04	0.10
Ibid.	Japan	Chu-Shikoku	Women	1991-1998	2.02	1.58	63	5.27	1.92	63	27.0	1.92	63	0.07	0.20
Ibid.	Japan	Kyushu-Okinawa	Women	1991-1998	1.71	1.62	67	4.10	1.74	67	20.9	1.89	67	0.08	0.20

Analyses were by graphite furnace atomic absorption spectrometry, unless otherwise specified. Cd-B, Cd-Ucr and Cd-D stand for Cd in blood (unit, μg/l), in urine as corrected for creatinine (unit, μg/g creatinine) and in 24-h food duplicate (unit, μg/day) unless otherwise specified

[a] 4–10-year-old, boys and girls mixed

[b] 28–46-year-old

[c] By inducstively coupled plasma-mass spectrometry

[d] Estimated from market basket-based data of Matsuda [18]; see the "Materials and Methods" section for details of estimation procedures

Analysis for Lead in Blood

For graphite furnace atomic absorption spectrometry (GFAAS) analysis, 100 μl blood sample was taken into an acid-washed tube and mixed with 900 μl of a 1 to 1 mixture of 10% Triton X-100 in water and 10% diammonium hydrogenphosphate in water. An aliquot, 10 μl, of the final mixture was introduced into a GFAAS system by use of an auto-sampler. The GFAAS was Hitachi type Z-8270 (Hitachi-naka, Hitachi, Japan) equipped with a tube-type cuvette, and the measurement was made at 283.3 nm using the standard addition method as previously described [27]. The average of two measurements was taken as a representative value.

Inductively coupled plasma-mass spectrometry (ICP-MS) analysis was conducted after acid digestion of 0.1 ml of blood sample by heating by microwave in a closed container, and the digest was taken up with ultra-pure water (final volume; 5 ml), and analyzed by the method as previously described [11].

Statistical Analysis

Log-normal distributions were assumed for Cd and Pb in food, blood or urine so that geometric means (GMs) and geometric standard deviations (GSDs) were taken as representative parameters for the distributions. In case original data were given in terms of arithmetic means (AMs) and arithmetic standard deviations (ASDs), they were converted to GMs and GSDs by use of the moment method [28] for uniformity of data presentation.

In case only medians were given in original articles, the medians were taken as if they had been GMs. Possible significant correlation between two parameters was examined by simple regression analysis. Smirnov test for extreme values was applied as necessary.

Results

Quantitative Correlation Between the Measures by GFAAS and ICP-MS

In order to compare the results by GFAAS analysis with that by ICP-MS, 20 blood samples of various Pb concentrations (24.0–42.8 μg/l blood by ICP-MS) were analyzed for Pb by both methods. When the results (in μg Cd/l blood) by the ICP-MS and GFAAS methods were taken on the x- and y-axis, respectively, there was a significant correlation between the paired results with a regression line of $y=0.677+0.77x$ ($r=0.797$, $p<0.01$). The analysis showed that while the correlation between the two sets of the results were close and significant, the difference between the two values were significant ($p<0.01$ by paired t test). Comparison of the AM values (29.4 and 23.3 μg Cd/l blood by the ICP-MS and GFAAS, respectively) suggests that ICP-MS would give greater values than GFASS by 26%.

Availability of the Data

Literature survey for publications in 1990s and 2000s for a combination of Pb-B (or Pb-U) and Pb-D, or Cd-B (or Cd-U) and Cd-D gave 14 reports on Pb and 15 reports on Cd, as summarized in Table 1 (for Pb) and Table 2 (for Cd). The basic parameters on data availability are presented in Table 3.

Table 3 Basic parameters of distribution

	A Pb (14 reports)												B Cd (15 reports)											
Parameter	Pb-B			Pb-U$_{cr}$			Pb-D			Ratio				Cd-B			Cd-U$_{cr}$			Cd-D			Ratio			
	GM (μg/l)	GSD	N[b]	GM (μg/g cr)	GSD	N[b]	GM (μg/day)	GSD	N[b]	Pb-B over Pb-D	Pb-U$_{cr}$ over Pb-D	Pb-D over Pb-B	Pb-D over Pb-U$_{cr}$	GM (μg/l)	GSD	N[b]	GM (μg/g cr)	GSD	N[b]	GM (μg/day)	GSD	N[b]	Cb-B over Cb-D	Cb-U$_{cr}$ over Cb-D	Cb-D over Cb-B	Cb-D over Cb-U$_{cr}$
N[a]	68	67	68	13	13	13	68	59	68	68	13	68	5.2	68	67	68	20	20	20	68	64	68	68	20	68	20
AM	30.3	1.5	59.7	3.7	2.4	66.8	18.3	2.1	34.7	2.3	0.3	0.7	52.9	2.13	1.56	80.1	3.16	1.79	122.7	27.6	1.81	56.4	0.09	0.20	13.4	8.2
ASD	13.8	0.2	146.3	2.0	0.6	33.4	12.1	0.6	25.0	1.7	0.3	0.5	42.8	1.15	0.22	163.0	1.69	0.26	121.3	19.2	0.36	80.5	0.04	0.14	5.2	7.2
MED	27.7	1.44	36	3.55	2.48	51	16.4	1.95	26	2.0	0.3	0.5	61.0	1.99	1.51	39	3.11	1.74	79	23.3	1.74	34	0.1	0.2	13.1	6.1
Min	11.8	1.08	16	1.23	1.51	36	2.2	1.36	10	0.5	0.1	0.1	19.7	0.29	1.21	16	0.64	1.39	36	5.64	1.25	10	0.0	0.0	3.5	1.8
Max	79.0	2.2	1227	7.0	3.6	145	56.7	4.4	145	11.1	1.1	2.0	53.9	4.84	2.35	1227	7.78	2.38	569	92.3	2.88	569	0.3	0.5	30.2	32.2

[a] Number of data sets

[b] Number of cases studied in each report

In the 14 reports on Pb, 68 pairs of Pb-B and Pb-D were available, but some papers did not give variation parameters such as GSD. The number of articles reporting Pb-U in combination with Pb-D was limited (13 papers). The distribution of the reported values for Pb-D was markedly skewed, but the AM was about 18 μg/day with the maximum of 56.7 μg/day. The highest GM for Pb-B was 79.0 μg/l.

In case of Cd for which 15 reports were available, 68 pairs of Cd in blood (Cd-B) and in food duplicates (Cd-D) were found. Reflecting the fact that the populations studied were residents in non-polluted areas, the average Cd-D was less than 30 μg/day, but the maximum was as high as 92.3 μg/day. The number of articles reporting both Cd-U and Cd-D was limited to 20. The average and the maximum Cd-U_{cr} were 3.16 and 7.78 μg/g cr, respectively.

Relation of Pb-D with Pb-B and with Pb-U

Regression analysis was conducted (taking Pb-D as an independent variable and Pb-B or Pb-U_{cr} as a dependent variable) to examine the quantitative effects of Pb-D on Pb-B as well as Pb-U_{cr}. The analysis with Pb-B (Eq. 1 in Table 4, Fig. 1) showed that there was a significant correlation between the two parameters ($r=0.360$, $p<0.01$), as expected. Only 13 cases were available for Pb-U_{cr}. The correlation of Pb-U_{cr} with Pb-D was weak and insignificant ($p>0.10$; Eq. 2 in Table 4), but that with Pb-B was close and significant ($p<0.01$; Eq. 3).

With Pb-B and Pb-D as an independent and a dependent variable, respectively (Eq. 4 in Table 4), the correlation was significant ($p<0.01$), and the slope was positive [0.317 (μg/daily diet per μg/l blood) with the 95% range of 0.115 and 0.517]. The observation as a whole was taken to suggest that Pb-D can be estimated from Pb-B, but the variation may be wide.

In fact, when the Pb-D over Pb-B ratio was taken as a dependent variable (with Pb-B as an independent variable) (Eq. 5 in Table 4), the slope (the 95% range) was negative, i.e. −0.011 (−0.018 to −0.003) suggesting that the role of Pb-D would decrease when total body burden (Pb-B as an indicator of the total body burden) be high. In other words, the non-dietary burden such as exposure to Pb-polluted atmospheric air may gain weight, as a function of total body burden, as to be discussed later.

An attempt was made to estimate the Pb-D (GM) that would induce Pb-B at given levels, such as 15 μg/l [the typical Pb-B level among current day Japanese women; the three lines for ref. 11 in Table 1], taking advantage of the regression analysis with Pb-B (GM) as an independent variable and Pb-D (GM) as a dependent variable as described previously (Fig. 1). The three crosses of a hypothetical vertical line at 15 μg/l with the regression line (and the 95% range curves in parenthesis) gave Pb-D of 14 (10–18) μg/l. Similar regression analysis taking Pb-B (GM) on the horizontal axis and Pb-D (GSD) on the vertical axis gave a regression line (Eq. 6 in Table 4) in which the slope was shallow but significant. The regression equation gave about 2.3 for 15 μg/l Pb-B. The factor of 2.3 may suggest a 68% variation range for Pb-D on an individual basis (Fig. 2).

The Pb-B over Pb-D ratios were calculated for each case with Pb-B in μg/l and Pb-D in μg/day, and listed in the second right-most column in Table 1. A regression analysis was conducted taking Pb-B (inμg/l) as an independent variable and the Pb-B over Pb-D ratio as a dependent variable. A case with the Pb-B over Pb-D ratio of 11.14 was excluded as an extreme value after application of Smirnov test. The calculation with 67 cases gave a regression line with $r=0.210$ ($p<0.10$), a slope=0.020 (the 95% range; 0.000 to 0.044) and an intercept=1.588 (Eq. 7 in Table 4); the correlation coefficient of 0.210 was of borderline

Table 4 Parameters of regression equations

Equation no.	Indepen-dent variable	Dependent variable	Intercept	Slope		No. of cases	Correlation coefficient|	P
			(α)	(β)	(95% interval)			
Eq. 1	Pb-D	Pb-B	22.810	0.41	0.15 – 0.670	68	0.360	<0.01
Eq. 2	Pb-D	Pb-U$_{cr}$	2.645	0.07	−0.049 – 0.19	13	0.37	>0.10
Eq. 3	Pb-B	Pb-U$_{cr}$	−0.120	0.14	0.05 – 0.240	13	0.7	<0.01
Eq. 4	Pb-B	Pb-D	8.737	0.32	0.12 – 0.519	68	0.360	<0.01
Eq. 5	Pb-B	Pb-D over Pb-B	0.998	−0.011	−0.018 – 0.003	68	0.32	<0.01
Eq. 6	Pb-B	Pb-D (GSD)	2.447	−0.010	−0.022 – 0	59	0.21	>0.10
Eq. 7	Pb-B	Pb-B over Pb-D	1.588	0.020	0.000 – 0.041	67[a]	0.210	<0.10
Eq. 8	Cd-D	Cd-B	0.810	0.05	0.04 – 0.06	68	0.79	<0.01
Eq. 9	Cd-B	Cd-D	−0.343	13.16	10.47 – 15.66	68	0.79	<0.01
Eq. 10	Cd-D	Cd-U$_{cr}$	1.7	0.070	0.020 – 0.12	20	0.570	<0.01
Eq. 11	Cd-U$_{cr}$	Cd-D	6.22	4.62	1.32 – 7.916	20	0.570	<0.01
Eq. 12	Cd-B	Cd-D over Cd-B	14.950	−0.711	−1.802 – 0.38	68	0.16	>0.10
Eq. 13	Cd-U$_{cr}$	Cd-D over Cd-U$_{cr}$	14.101	−1.871	−3.777 – 0.03	20	0.44	<0.10

Unless otherwise specified, Pb-B, Pb-Ucr, Pb-D, Cd-B, Cd-Ucr and Cd-D are GM values in μg/l, μg/g cr or μg/day

[a] One case with the Pb-B over Pb-D ratio of 11.14 was depeted as an extreme value after Smirnov test for extreme value

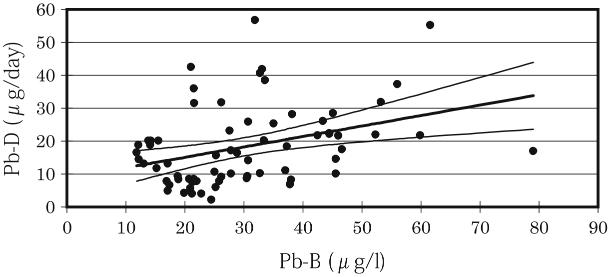

Fig. 1 Relation of Pb in blood and Pb in daily diet. A regression analysis was conducted with Pb in blood (*Pb-B*) as an independent variable and Pb in daily diet (*Pb-D*) as a dependent variable. Both Pb-B (μg/l) and Pb-D (μg/day) are GM values for the study sites. The *line* in the middle is a calculated regression line (for the equation parameters, see Table 4), and the *curves* on both sides are the 95% ranges of the means. Each *dot* represents one study site

significance ($p<0.10$). Based on the equation, the best estimate of the Pb-B over Pb-D ratio for Pb-B of 15 μg/l was 1.9 or about 2.

Dietary Burden and Internal Dose of Cd

The correlation analysis showed that Cd-B correlated significantly ($p<0.01$) with Cd-D, with a significant correlation coefficient of 0.792 (Eq. 8 in Table 4). When Cd-B was taken as an independent variable, the lower 95% limit of the slope (β) was 10.47, which was clearly positive (i.e. >0) (Eq. 9 in Table 4, Fig. 3).

The number of studies of Cd-U paired with daily dietary intake data was limited and only 20 pairs of Cd-U_{cr} and Cd-D were available. Similar analysis revealed that, taking Cd-D and Cd-U_{cr} as an independent and a dependent variable, respectively, the slope was positive (0.070) suggesting that Cd-U would increase as an increasing function of Cd-D (Eq. 10 in Table 4). The correlation, $r=0.570$, was statistically significant ($p<0.01$) (Fig. 4).

The analysis taking Cd-B as an independent variable and the ratio of Cd-D over Cd-B as a dependent variable (Eq. 12 in Table 4) revealed that the ratio stayed essentially unchanged with no response to an increase in Cd-B. Although the correlation ($r=0.158$) was weak and statistically insignificant ($p>0.10$), the 95% range for the slope was −1.802 to 0.381, indicating that the regression line was essentially in parallel to the horizontal axis. A similar

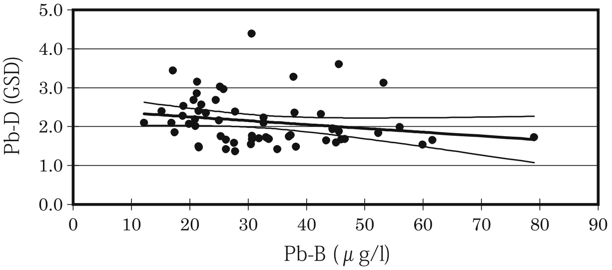

Fig. 2 No significant changes in GSD of Pb in daily diet as a function of Pb in blood. A regression analysis was conducted with Pb in blood (*Pb-B*; GM in μg/l for the study site) as an independent variable and GSD (dimensionless) of Pb in daily diet (*Pb-D*) as a dependent variable. The meaning of the *line* in the middle and two *curves* on both sides, as well as that of the *dots* are as in Fig. 1. For equation, see Table 4

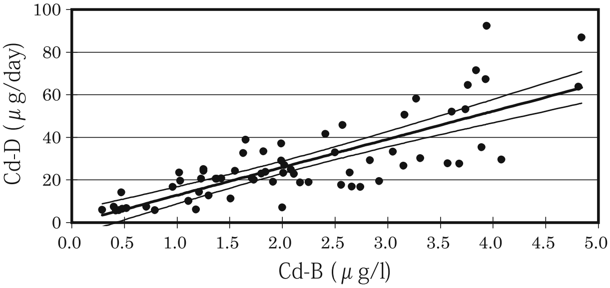

Fig. 3 Relation of Cd in blood and Cd in daily diet. A regression analysis was conducted with Cd in blood (*Cd-B*) as an independent variable and Cd in daily diet (*Cd-D*) as a dependent variable. Both Cd-B (μg/l) and Cd-D (μg/day) are GM values for the study sites. The meaning of the *line* in the middle and two *curves* on both sides, as well as that of the *dots* are as in Fig. 1. For equation, see Table 4

analysis with Cd-U_{cr} and the ratio of Cd-D over Cd-U_{cr} (Eq. 13) also gave a regression line with no significant increase of the ratio with increasing Cd-U_{cr}.

Discussion

It appears to be the case that 50 to 100 μg/l is a critical concentration when GFAAS is employed for Pb-B analysis; for example, a coefficient of variation as large as 20% was reported when blood samples containing 100 μg Pb/l was analyzed [29]. As the target Pb-B concentrations in the present study were well below these levels (e.g. Table 1), it was thought essential to make a compatibility analysis in results between conventional GFAAS and newly developed ICP-MS. The results showed that there was a close correlation between the GFAAS results and ICP-MS result, and that ICP-MS would give greater values than GFAAS by 26%. In contrast, GFAAS has been well accepted for both Cd-B and Cd-U analyses in a wide range [30], suggesting no need for compatibility tests with other analytical methods in case of Cd analyses.

The present analyses with data in 14 reports on Pb and 15 reports on Cd in blood, urine and 24-h diet samples suggested that it should be possible to estimate both Pb-D and Cd-D

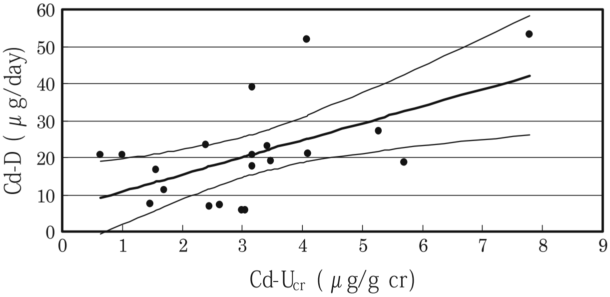

Fig. 4 Relation of Cd in blood and Cd in daily diet. A regression analysis was conducted with Cd in urine after correction for creatinine (*Cd-U_{cr}*) as an independent variable and Cd in daily diet (*Cd-D*) as a dependent variable. Both Cd-U_{cr} (μg/g cr) and Cd-D (μg/day) are GM values for the study sites. The meaning of the line in the middle and two curves on both sides, as well as that of the dots are as in Fig. 1. For equation, see Table 4

from Pb-B and Cd-D. The Cd-B-based estimation for Cd-D appears to be quite possible as the Cd-D over Cd-B ratio stayed unchanged irrespective of Cd-B. It was also the case when Cd-U_{cr} was employed in place of Cd-B. In contrast, the estimation for Pb-D from Pb-B apparently needs careful evaluation of concurrent intensity of exposure to Pb, because the ratio of Pb-D over Pb-B may decrease as a function of increasing intensity of Pb exposure as represented by Pb-B (Eq. 7 in Table 4).

Such difference between Cd and Pb in the relationship of dietary exposure (Cd-D and Pb-D) with total body burden (as expressed by Cd-B or Cd-U_{cr}, and Pb-B) is in agreement with previous observation on the populations environmentally exposed to Pb and Cd. Namely, the exposure to Cd is almost exclusively via foods as Cd in the atmosphere is generally very low and contributes little to total body burden [2], whereas contribution of air-borne Pb may exceed 50% of total Pb burden even for general populations [2] as a function of the extent of urban air pollution with Pb [1]. In this sense, the gap between the 1980’s studies-based estimate by Carrington et al. [31, 32] and the present estimation as to be discussed below may be attributable to the different intensity of environmental Pb pollution, especially that of urban air.

Based on the studies of Ryu et al. [33] and Sherlock et al. [34–36], Carrington et al. [31] estimated 10, 10, 30 μg Pb/100 ml blood (or 100, 100 and 300 μg Pb/l blood) as Pb-B levels of concern for children, pregnant women and adults and figured out Pb-D of 60, 250 and 750 μg Pb/day by use of conversion factors [=Pb-B (inμg/100 ml)/Pb-D (in μg/day) [31]] of 0.16, 0.04 and 0.04 for the three groups, respectively. The Pb-D of 750 μg/day is however apparently too high when the present day Pb-D is considered; for example, the Pb-D level is well below 60 μg/day in Japan (Table 1). Pb-B has also been reduced to <20 μg/l (or <2 μg/100 ml; Table 1). Thus, the conversion factor of 0.04 (or 0.40 when Pb-B is expressed in μg/l) for adults for example, will be no longer valid.

The present analysis made it clear in addition, that the relation of Pb-B with Pb-D is not constant but may vary as a function of Pb-B (Eq. 7 in Table 4) so that the ratio, calculated as Pb-B (inμg/l) over Pb-D (inμg/day) e.g. for adult Japanese women with current Pb-B of around 15 μg/l (in the three lines under ref. 11 in Table 1) should be around 1.9 (Eq. 7 in Table 4) as described above. For those with Pd-B of about 30 μg/l, the best estimate will be 2.2 (Eq.7 in Table 4). No data are available to compare the ratio for children directly with that for adult people in Japan. Nevertheless, the data made available by Moon et al. [7] based on the study in Busan, Korea, suggest that the ratio for children may be twice as high as that for their mothers (Table 1).

Possible effects of insufficient calcium (Ca) intake on Pb-B among children have been a matter of concern in recent years. Three reports are available which unanimously suggest that Pb-B would be higher among those who take Ca only insufficiently. In a study in Mexico city [37] in which 200 cases of children (at the age of <13 to 50+ months) were analyzed, those (n=50 each) with daily Ca intake of <360, 360 to <449, 449 to <624 and 624 mg/day (estimated by food intake frequency questionnaires) had Pb-B [GM estimated from AM and ASD by the moment method [28]] at 9.75, 9.03, 8.00 and 7.64 μg/100 ml, respectively. P-values for the differences in Pb-B from the lowest Ca intake group were >0.10, >0.10, <0.10 and <0.05, respectively.

Elias et al. [38] reported that Pb-B [2.96 μg/100 ml as GM estimated by the moment method [28]] of 225 primary school children (in Kuala Lumpur, Malaysia) decreased as a reverse function of dietary Ca intake (407 mg/day as AM estimated by food frequency questionnaire); the slope (with Ca intake and Pb-B on the horizontal and vertical axis, respectively), was <0 (i.e., −0.011) with p=0.014. In a village in Mexico, a study [39] on 752 residents including 202<15 year-old children showed that Pb-B was lower (7.2, 6.9

and 6.0 μg/100 ml as GM, respectively) among those (n=243 to 247) who took more Ca (i.e. 505, 505–706, and 706 mg/day; estimated by food frequency questionnaires).

It is known through national surveys that Ca intake is insufficient especially among young children in Japan [26]. Thus, more than 50% of children at the ages of 1–2 and 3–5 years take Ca less than the adequate intake (AI; 40), and the median intake is about the AI at 6–9 years of age [26]. Thus, insufficient intake of Ca among children should be taken as a dietary factor to increase sensitivity of Japanese children to Pb toxicity. Of interest in this connection is the observation that Pb in Ca supplements does not affect Pb-B, possibly because Pb absorption in the digestive tract is suppressed by co-existing abundant Ca in the pellets [41].

Different from adult cases, poor personal hygiene of using dirty hands when eating foods is an additional factor to increase lead exposure of children. Freeman et al. [42] observed increased Pb burden through foods such as banana and hot dog when taken with spoilt hands.

There are several limitations in the present analysis. Compared with the number of pairs of Cd-D and Cd-B (60 in total), only 13 pairs were available for the analysis between Cd-D and Cd-U. More data are apparently desired to examine possible association between Cd-D and Cd-U, because urine samples are more readily available than blood samples in field surveys. In the case of Pb, the limited number for Pb-U is not necessarily a matter of serious concern in evaluation because poor correlation of Pb-U with Pb-B is well-known especially when Pb exposure is low [43].

It was observed in the present study that the ICP-MS would be give values about 26% larger than the values by GFAAS. Another factor to induce bias relates to the methods to estimate recent metal burden for Japanese populations. The market basket method was employed by Matsuda [18] to establish the estimates, whereas the food duplicate method was employed in other studies. The difference might induce systematic bias in evaluation. For example, the data by Watanabe et al. [12] on 1990 survey gave a number weighted average of 19.1 μg/day for Pb. It was 40.8 μg/day for Cd. In contrast, Toyoda et al. [44], using the market basket method assumedly similar to that used by Matsuda [18], reported that daily Pb and Cd intakes by Japanese population in 1990 were 41 μg/day and 26 μg/day, respectively. In estimating the Pb-B over Pb-D ratios based on Kaji [17], Takagi et al. [19] Ikeda et al. [11], the estimation of dietary intake was based on Matsuda [18]. In Takagi [19] and Ikeda et al. [11], Pb-B for example was measured by the ICP-MS method. Introduction of factors for converting a market basket-based value to a food duplicate-based one (e.g. division by factor 2) and a ICP-MS-based value to a GFASS-based value (-ca. 20%) would give Pb-B (in μg/l) over Pb-D (in μg per day) ratio of 1.3 to 2.0 for Kaji [17], 1.1 for Takagi et al. [19] and 1.1 to 1.2 for Ikeda et al. [11].

In over-all evaluation, it appears prudent to conclude that dietary intake of Pb and Cd can be estimated from Pb and Cd in blood, as well as Cd in urine. Nevertheless, care should be taken for the estimation of Pb-D from Pb-B as the ratio of Pb-D over Pb-B may increase as Pb-B decreases. The best estimate for Pb-B (μg/l)/Pb-D (μg/day) will be about two for adults, and the ratio for children may be higher possibly by a factor of about two [7]. It should be noted that in the case of children, poor personal hygiene and possible effects of nutritional factors such as insufficient calcium intake (typically in Japan) may need to be taken into consideration.

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Conflicts of Interest The authors declare that they have no conflicts of interest.

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