CADMIUM EXPOSURE IN THAI POPULATIONS FROM CENTRAL, NORTHERN AND NORTHEASTERN THAILAND AND THE EFFECTS OF FOOD CONSUMPTION ON CADMIUM LEVELS

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Abstract. The aim of the present study was to investigate the association between cadmium body burden and the areas of exposure in Thailand, as well as blood pressure levels, the types and frequencies of foods, and alcohol consumption. A total of 182 healthy adult Thai subjects of both genders (89 males, 93 females) ages 18 to 57 years old weighing 40-95 kg were included in this study. Participants were residents from three main areas of Thailand: Pathum Thani Province (central Thailand; *n*=50), Khon Kaen Province (northeastern Thailand; *n*=43) and Mae Sot District, Tak Province (northern Thailand; *n*=89). The total amount of cadmium excreted in urine over 2 hours (μg/g creatinine) was used as an indicator of long-term cadmium exposure. Quantitation of cadmium was performed using electrothermal (graphite furnace) atomic absorption spectrometry (GFAAS). The urinary cadmium excreted displayed a normal frequency of distribution. Significantly higher mean cadmium levels were observed in subjects residing in Mae Sot, Tak Province (0.63 ± 1.41 μg/g creatinine) and Khon Kaen (0.51 ± 0.76 μg/g creatinine) compared to Pathum Thani Province (0.23 ± 0.35 μg/g creatinine). The proportion of subjects with elevated blood pressure was significantly higher in the group exposed to higher (*n*=39) as opposed to lower (*n*=5) levels of cadmium. There were no significant differences in the mean total amounts of cadmium excreted in the 2-hour urine samples from subjects who consumed different types of meat and offal, or from those who consumed them at different frequencies.

INTRODUCTION

Cadmium is a toxic and carcinogenic metal of increasing public health concern. In the general population, the primary sources of cadmium exposure are cigarette smoke, food intake (shellfish, offal, certain vegetables), and ambient air, particularly in urban areas and in the vicinity of industrial settings (International Agency for Research on Cancer (IARC), 1993; Satarug *et al*, 1996; Baker *et al*, 2001; Ujjin *et al*, 2002; Nordberg *et al*, 2005; Agency for Toxic Substances and

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Disease Registry, (ATSDR, 2007). It exhibits higher rates of soil to plant transference than other toxic metals, such as lead and mercury, which makes it present in most human foodstuffs albeit in low quantities.

Cadmium is absorbed into the body from dietary sources and cigarettes *via* enteral and pulmonary routes. It accumulates in various tissues and organs with the most extensive accumulation occurring in the renal cortex. Cadmium nephrotoxicity has been detected at renal cadmium concentrations of ≥50 μg/g wet tissue weight (Satarug *et al*, 2000, 2003). Cadmium persists in the kidney of humans for many years (half-life of 30 years). This provides ample opportunity for cadmium toxicity to occur with no additional exposure. Approximately 0.001% of cadmium in the body is excreted per day, mostly in urine. The extremely slow excretion rate of cadmium is due to a lack of an active biochemical mechanism for elimination of cadmium coupled with renal reabsorption. The net result is an accumulation of cadmium in the body, notably in the liver and kidneys. Cadmium exposure induces hypertension in animal models (Schroeder and Vinton, 1962; Satarug *et al*, 2006). In occupationally and environmentally exposed populations, cadmium is nephrotoxic, inducing tubular and glomerular dysfunction (Jin and Joseph-Quinn, 2004; Åkesson *et al*, 2005; ATSDR, 2007). Epidemiologic studies of the association between environmental cadmium exposure and blood pressure end points are inconsistent. Although some studies found positive associations (McKenzie and Kay, 1973; Vivoli *et al*, 1989; Whittemore *et al*, 1991; Pizent *et al*, 2001), other studies found null or even inverse associations (Beevers *et al*, 1976; Kagamimori *et al*, 1986; Staessen *et al*, 1984, 1991).

The objective of the present study was to investigate cadmium exposure in Thai populations in central, north and northeastern Thailand, and the effects of food consumption on cadmium levels.

MATERIALS AND METHODS

Study subjects and study site

The study was conducted in the three regions of Tahiland: central Thailand (Pathum Thani Province), northeastern Thailand (Khon Kaen Province), and northern Thailand (Mae Sot, Tak Province). The study protocol was approved by the Ethics Committee of the Faculty of Medicine, Khon Kaen University and the Ministry of Public Health for Thailand. Written informed consent was obtained from each volunteer after being informed about the study objectives and procedures. A total of 182 (89 males, 93 females) healthy Thai subjects age 18 to 55 years old were recruited into the study. A questionnaire, the methods for systematic collection, and interview guidelines were developed in consultation with local public health physicians, officers and epidemiologists. The survey covered demographic data (age, gender, height, body weight), residency period, ethnic background, general health, history of chronic diseases, pregnancy status, the use of oral contraception, the use of herbal medicine, smoking and drinking habits, and selected food frequencies. Dietary information was collected on a range of foods. The emphasis was on foods other than rice known to contain higher than usual levels of cadmium, such as meat (chicken, duck, pork, fish, sea food) and offal (liver and kidney). Body weight (in kilogram) was measured. The blood pressure was measured by a physician with the subject in the seated position using a standard mercury sphygmomanometer.

Subjects were excluded from the study if they had one of the following criteria: a clinically significant history of or current liver or renal disorders, cardiovascular disease, diabetes, hyperlipidemia, a family history of hypertension, history of being a metal worker, or were pregnant or breast-feeding.

Urine sample collection

Urine samples were collected from all volunteers. The volume of urine was measured and 5 mililiters was collected in a 10-ml polypropylene tube before being stored at -20ºC until analysis.

Determination of urinary cadmium levels

Quantification of cadmium excreted in the urine over 2 hours was carried out using electrothermal (graphite furnace) atomic absorption spectrometry (GFAAS) according to the method of Edwin *et al* (Wang, 1998). The equipment consisted of a Perkin-Elmer atomic absorption spectrometer, model 4100 ZL, equipped with a transversely-heated electrothermal atomization unit, a longitudinal Zeeman-effect background correction system, and a model AS-71 autosample. Transversely-heated graphite atomizers with integrated platforms were used after proper conditioning according to the manufacturer's recommendations. A cadmium hollow-cathode lamp (Varian), operating at 6 mA, was used at the 228.8 nm cadmium line.

Data and statistical analysis

Statistical analysis was performed using SPSS version 12.0. (Lead Technologies). The Kolmogorov-Smirnov goodness of fit test was used to test conformation of normal distribution of measured data. Association between measured variables was analysed by correlation analysis using the Pearson's correlation test or the Spearman's rank correlation test, where appropriate. The one-way ANOVA or Kruskall-Wallis one-way ANOVA were used to explore statistically significant differences in mean or median values for test variables in the three groups. The Student's *t*-test or Mann-Whitney sum rank test were used to determine statistically significant differences between the two groups. Comparison of qualitative data was done by the chi-square test. Statistical significance was set at $\alpha = 0.05$ for all tests.

RESULTS

Characteristics of the study population

Table 1 summarizes the demographic data for all subjects (age, body weight, blood pressure, occupation and areas of exposure). The systolic and diastolic blood pressure ranges were 90-150 and 50-110 mmHg, respectively. The majority of study subjects were students (52.1%); other occupations included farmers (13.7%), daily laborers (12.1%), hospital workers (5.3%), mechanics (3.7%), officials (2.1%), housewives (2.1%), factory workers (1.6%), laborers (1.1%) and janitors (0.5%). Fifty-seven (31%), 85 (45%) and 40 (22%) of these subjects were residents of Pathum Thani, Tak (Mae Sot District), and Khon Kaen Province, respectively.

Table 2 summarizes food and alcohol consumption for all the subjects. The consumption of pork and fish constituted the highest prevalence of food (79.5%), followed by chicken (77.4%), sea food (76.8%), liver (64.2%), duck (50%) and kidney (37.9%). For each type of foodstuff, the highest frequencies for consumption were 1, 2-3, 2-3, 2-3, and 2-3 days per week were observed for seafood, chicken, pork, fish and duck, respectively. The proportions of subjects who were regular (>1 day/week) consumers of alcohol (including beer, wine and/or fermented rice) were approximately 88 and 53% for males and females, respectively.

Frequency distribution of urinary cadmium excretion

Fig 1 shows the frequency distribution of total cadmium excreted in the urine over 2 hours (logarithmically transformed) for all subjects. The frequency of urinary cadmium

Table 1
Demographic data for all subjects included in the study. Data are presented as mean ± SD and (range) or number (percent) values.

Parameters	Total subjects (N = 182)	Males (n = 89)	Females (n = 93)
Number of subjects, n (%)	182 (100%)	89 (48.9%)	93 (51.1%)
Age (years)	29.0 ± 10.3 (18-57)	30.3 ± 10.6 (18-57)	27.8 ± 10.0 (18-52)
Body weight (kg)	58.1 ± 10.6 (40.0-95.0)	62.3 ± 8.7 (45.0-92.0)	54.2 ± 10.7 (40.0-95.0)[a]
Blood pressure (mmHg)			
Systolic BP	117 ± 15(90-160)	110 ± 16(90-140)	107 ± 13 (90-150)
Diastolic BP	75 ± 12(50-110)	70 ± 12(50-90)	70±9 (50-100)
Occupation, n (%)			
Student	99 (52.1)	42 (21.5)	57 (29.2)
Wage earner	23 (12.1)	11 (5.8)	12 (6.2)
Hospital worker	10 (5.3)	7 (3.7)	3 (1.6)
Mechanic	7 (3.7)	2 (1.0)	5 (2.6)
Official	4 (2.1)	3 (1.5)	1 (0.5)
Janitor	1 (0.5)	1 (0.5)	0 (0.0)
Factory worker	3 (1.6)	1 (0.5)	2 (1.0)
Housewife	4 (2.1)	0 (0.0)	4 (2.1)
Farmer	26 (13.7)	16 (8.2)	10 (5.1)
Laborer	2 (1.1)	2 (1.1)	0 (0.0)
Areas of exposure, n (%)			
Pathum Thani	57 (31.3)	19 (21.3)	38 (40.9)
Tak (Mae Sot)	85 (46.7)	49 (55.1)	36 (38.7)
Khon Kaen	40 (22.0)	21 (23.6)	19 (20.4)

[a]Statistically significant difference in males with $p < 0.05$ (Student's t-test).

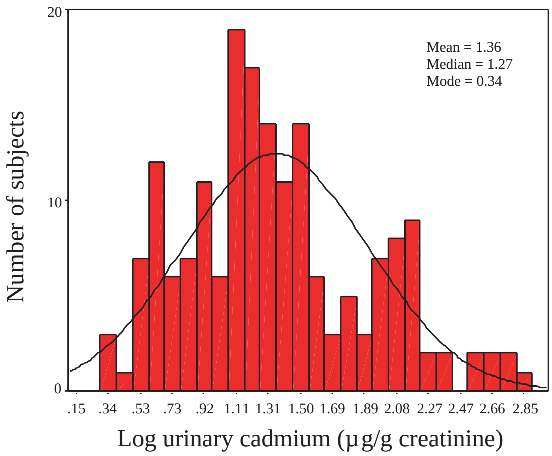

Fig 1–Frequency of distribution of logarithmically transformed cadmium excreted in the urine over 2 hours (µg/g creatinine).

excreted was normally distributed, as judged by a test for goodness of fit with mean, median and mode values of 1.36, 1.27 and 0.34 ng/2 hr, respectively (Kolmogorov-Smirnov goodness of fit test, $p < 0.05$).

Cadmium body burden in relation to areas of exposure

Fig 2 presents the mean total amounts of cadmium excreted in the 2-hour urine test (µg/g creatinine) for subjects from the three studied areas of Thailand (Pathum Thani, Tak and Khon Kaen Province). Significantly higher amounts of cadmium were observed in subjects resided in Mae Sot, Tak Province (0.63 ± 1.41 µg/g creatinine) and Khon Kaen

Table 2
Food and alcohol consumption in the study population. Data are presented as numbers and percentages.

Parameters		Total subjects (N = 182)	Males (n = 89)	Females (n = 93)
Types of foodstuffs, n (%)				
Liver		122 (64.2)	60 (30.8)	62 (31.8)
Kidney		72 (37.9)	41 (21.0)	31 (15.9)
Seafood		146 (76.8)	74 (37.9)	72 (36.9)
Meat:	Chicken	147 (77.4)	69 (35.4)	78 (40.0)
	Pork	151 (79.5)	72 (36.9)	79 (40.5)
	Fish	151 (79.5)	73 (37.4)	78 (40.0)
	Duck	95 (50)	38 (19.5)	57 (29.2)
Frequency of consumption, n (%)				
Seafood:	1 day/week	69 (36.3)	34 (17.4)	35 (17.9)
	2-3 days/week	46 (24.2)	24 (12.3)	22 (11.3)
	4-5 days/week	27 (14.2)	15 (7.7)	12 (6.2)
	Daily	4 (2.1)	1 (0.5)	3 (1.5)
Chicken:	1 day/week	30 (15.8)	16 (8.2)	14 (7.2)
	2-3 days/week	58 (30.5)	23 (11.8)	35 (17.9)
	4-5 days/week	42 (22.1)	20 (10.3)	22 (11.3)
	Daily	17 (8.9)	10 (5.1)	7 (3.6)
Pork:	1 day/week	7 (3.7)	4 (2.1)	3 (1.5)
	2-3 days/week	52 (27.4)	27 (13.8)	25 (12.8)
	4-5 days/week	42 (22.1)	19 (9.7)	23 (11.8)
	Daily	50 (26.3)	22 (11.3)	28 (14.4)
Fish:	1 day/week	32 (16.8)	13 (6.7)	19 (9.7)
	2-3 days/week	77 (40.5)	37 (19.0)	40 (20.5)
	4-5 days/week	28 (14.7)	16 (8.2)	12 (6.2)
	Daily	14 (7.4)	7 (3.6)	7 (3.6)
Duck:	1 day/week	1 (0.5)	0 (0.0)	1 (0.5)
	2-3 days/week	79 (41.6)	30 (15.4)	49 (25.1)
	4-5 days/week	4 (2.1)	3 (1.5)	1 (0.5)
	Daily	10 (5.3)	5 (2.6)	5 (2.6)
Frequency of alcohol consumption, n (%)				
	Not at all	55 (30.4)	11 (12.4)	44 (47.3)[a]
	1 time in 6 months	1 (0.5)	1 (1.1)	0 (0.0)
	1 day/week	86 (47.3)	46 (51.7)	40 (43.0)
	2-3 days/week	17 (9.3)	14 (15.7)	3 (3.2)
	4-5 days/week	20 (11.0)	15 (16.9)	5 (5.4)
	Daily	2 (1.1)	2 (2.2)	0 (0.0)

[a]Statistically significant greater proportion than in females with $p < 0.05$ (chi-square test).

(0.51 ± 0.76 μg/g creatinine), compared with Pathum Thani Province (0.23 ± 0.35 μg/g creatinine) (p = 0.03 *vs* 0.02).

Cadmium body burden in relation to blood pressure

Subjects were considered to have high

Table 3
Mean total amounts of cadmium excreted in the urine over 2 hours (μg/g creatinine) in individuals who consumed different types and frequencies of meat (pork, chicken, fish, seafood and duck), and offal (liver, kidney). Data are presented as number (*n*) and mean ± SD.

Food stuffs	Frequency	*n*	Total 2-hr urinary cadmium (μg/g creatinine)
Pork	< 3 days/week	55	0.55 ± 0.90
	> 3 days/week	89	0.58 ± 1.20
Chicken	< 3 days/week	83	0.66 ± 1.31
	> 3 days/week	57	0.43 ± 0.69
Fish	< 3 days/week	105	0.52 ± 1.04
	> 3 days/week	39	0.67 ± 1.23
Seafood	< 3 days/week	107	0.67 ± 1.28
	> 3 days/week	30	0.36 ± 0.68
Duck	< 3 days/week	80	0.34 ± 0.46
	> 3 days/week	11	0.51 ± 1.04
Liver	< 3 days/week	117	0.58 ± 1.15
	> 3 days/week	23	0.36.± 0.48
Offal	< 3 days/week	69	0.66 ± 1.15
	> 3 days/week	98	0.53 ± 1.06

blood pressure when diastolic and systolic blood pressures were greater than 90 and 150 mmHg, respectively. The proportion of subjects with high blood pressure was significantly higher in the group exposed to higher (39) as compared to lower (5) levels of cadmium ($p = 0.01$).

Cadmium body burden in relation to consumption of different types of foodstuffs and alcohol

Fig 3 shows mean total amounts of cadmium excreted in urine over 2 hours in subjects who consumed different types of meats (pork, chicken, fish, seafood and duck) at different frequencies (less than and more than 3 days/week). There were no significant differences in the mean total amounts of cadmium excreted in the urine over 2 hours among the subjects who consumed different types and different frequencies of meat and offal.

Table 3 summarizes mean total amounts of cadmium excreted in urine over 2 hours (ng/2 hr) in individuals who consumed different types and frequencies of meat and offal. There were no significant differences in urinary cadmium levels between individuals with frequent (>3 days/week) and infrequent (<3 days/week) meat consumption.

Cadmium body burden in relation to residential areas and offal consumption

In subjects who consumed kidney regularly, the mean total amount of urinary cadmium excretion in subjects who resided in Pathum Thani (0.60 ± 0.84 μg/g creatinine) appeared to be higher than that of those who resided in Khon Kaen Province (0.30 ± 0.38 μg/g creatinine).

DISCUSSION

In the present study, the total amount of cadmium excreted in the urine over 2 hours (μg/g creatinine) was used as an index of long-term cadmium exposure. Rela-

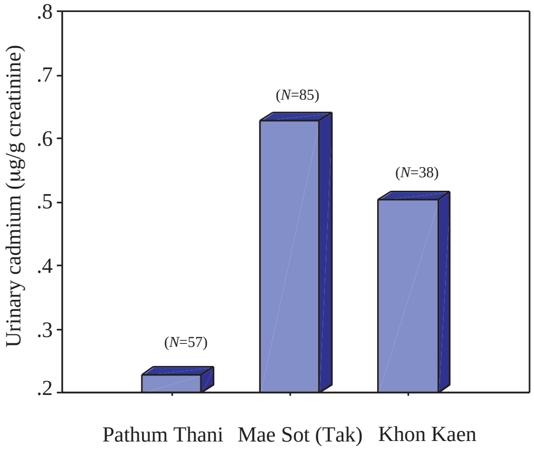

Fig 2–Influence of residential areas on mean total amounts of cadmium exposure levels (µg/g creatinine) in all subjects. The number of subjects (*n*) is shown in parentheses. Significantly higher than those who resided in Pathum Thani Province with $p < 0.05$ (Student's *t*-test).

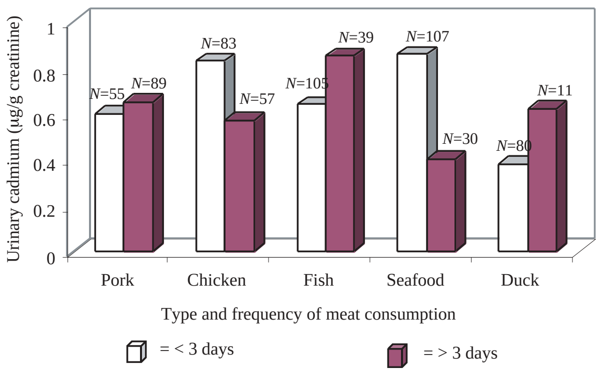

Fig 3–Mean total amounts of cadmium excreted in the urine over 2 hours (µg/g creatinine) in individuals who consumed different types and frequencies of meat. The numbers of subjects (*n*) are shown in parentheses.

tionships between cadmium body burden and consumption of foodstuffs and alcohol, blood pressure and area of exposure were investigated in a total of 182 healthy subjects residing in three different areas of Thailand. The results show that subjects who resided in Mae Sot District, Tak Province were exposed to about 2.5 times higher cadmium levels than those who resided in Bangkok. Mae Sot District, Tak Province has been reported as an area with high levels of cadmium. High levels of cadmium contaminated in rice and soil in Mae Sot District have been reported in 13 autopsies. This raises public health concern regarding exposure of inhabitants in this area to high levels of cadmium through their long-term daily consumption of rice (Swaddiwudhipong *et al*, 2007). Although statistically non-significant, the levels observed for inhabitants in Khon Khaen Province were also relatively high comparing to those of Bangkok. This may be related to the extent of consumption of meat and offal in this group of population. Cadmium concentrations in all subjects were classified into 3 levels: below 5 (*n*=54), 5-10 (*n*=77) and above 10 (*n*=84) µg/g creatinine, with mean±SD values of 3.95±0.96, 7.14±1.37, and 17.81±7.19 µg/g creatinine, respectively. Most subjects (172/182) had total cadmium excretion in the urine over 2 hours of less than the maximum tolerable internal dose for a non-exposed population of 2 µg/g creatinine, as defined by the World Health Organization. Eight and two subjects in Tak and Khon Kaen Province, respectively, had cadmium levels exceeding this.

Total urinary cadmium excretion appeared to be associated with high blood pressure status, although it is noted the total number in each group was small, especially in the group of subjects with high urinary excretion of cadmium. The proportion of subjects with elevated blood pressure was significantly higher in the group exposed to higher levels of cadmium. Chronic cadmium exposure is associated with a number of distinct pathological changes in a variety of tissues and organs, reflecting the multiplicity of cadmium toxicities (Satarug and Moore, 2004). This included tubular and glomerular dysfunction, chronic renal failure, stones, hypertension, osteoporosis, atherosclerosis, increased risk of diabetes and malignancies. With respect to the link between cadmium-induced tubular dysfunction and high blood pressure, chronic low-dose cadmium administration raised the blood pressure levels in dogs, rabbits, monkeys and various strains of rats. However, the mechanism by which cadmium induces a hypertensive phenotype in these animals is unknown. It should be noted that cadmium effects on blood pressure vary among species and strains of animals and by cadmium dose levels (Nomiyama *et al*, 2000). Satarug *et al* (2005) reported that higher cadmium exposure levels experienced by the subjects were associated with an increase in high blood pressure and signs of renal tubular damage. Subjects with an average urinary cadmium concentration of 10 nM (1.16 mg/l) face an 11% increase in the probability of having high blood pressure, whereas subjects with cadmium-linked NAG-uria (excreting >8 NAG enzyme units/ g creatinine) face a 20% increase in the probability of having high blood pressure.

Cadmium is an ubiquitous environmental pollutant of increasing world-wide importance due to its high rates of soil to plant transference. It is a by-product or a waste product of industrial production of zinc, lead and copper. High concentrations of cadmium can be found in soil in areas rich in zinc ore in which cadmium occurs naturally in great abundance along with lead and copper (Jarup *et al*, 2003). Food crops grown on cadmium containing soil constitute a major source non-workplace exposure to cadmium other than exposure from smoking cigarettes (Nasreddine and Parent-Maasin, 2002; Satarug *et al*, 2000, 2003). Offal, notably kidney and liver, and certain shellfish, usually contain high levels of cadmium (Storelli and Macrotigiano, 2001; Lukaszewicz *et al*, 2003). Therefore, high cadmium exposure can be expected to occur in frequent consumers of offal and shellfish. The differences in cadmium levels from different sources of food and in the residential areas found in this study could not be definitely identified since most subjects concurrently consumed other types of foodstuffs, and in addition, the cadmium content in the food samples consumed were not measured. However, it is noted that in subjects who consumed kidney regularly, the mean levels of urinary cadmium excreted by subjects who lived in Pathum Thani (0.60 ± 0.84 μg/g creatinine) appeared to be higher than those who lived in Khon Kaen Province (0.30 ± 0.38 μg/g creatinine). The proportion of subjects with no alcohol consumption was significantly higher in females than in males, but appeared to have no influence on urinary cadmium excretion.

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