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Biological Monitoring of Cadmium Exposed Workers in a Nickel-Cadmium Battery Factory in China

Guicheng ZHANG[1], Elaine LINDARS[1], Zeren CHAO[2], Yu BAI[2] and Jeff SPICKETT[1]

[1]School of Public Health, Curtin University of Technology, Australia and
[2]Xinxiang Occupational Medicine Institute, China

Abstract: Biological Monitoring of Cadmium Exposed Workers in a Nickel-Cadmium Battery Factory in China: Guicheng ZHANG, *et al.* School of Public Health, Curtin University of Technology—A cross-sectional study of renal damage in workers from a Chinese Ni-Cd battery factory is reported in this paper. The present exposure of surveyed workers to Cd may be likened to that of factories in developed countries prior to the 1950s. The results show urinary cadmium did not increase significantly with the years of exposure in aged workers exposed to cadmium. In these occupationally exposed workers urinary cadmium levels of 3 to 60 μg/g creatinine relate to between 15% and 20% of the workers having B_2-MG proteinura, and blood cadmium levels less than 5 μg//relate to more than 10% of the workers having B_2-MG proteinura. The results suggest that a urinary cadmium concentration of 5 μg/g cr or a blood cadmium concentration of 5 μg/ /would not be a safe level.
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Key words: Cadmium exposure, Workers, Biological measuring, Urine, Blood

In 1950 a large group of workers exposed to cadmium oxide dust in a battery factory were investigated[1], and it was found that prolonged exposure to cadmium gave rise to renal damage. Since then it has been well documented that exposure to cadmium will cause kidney impairment[2–4]. This is because cadmium accumulates predominantly in the kidneys as a result of the long biological half-time of 10–30 yr[3]. In the absence of renal damage, cadmium concentrations in urine generally reflect the amount of cadmium stored in the body[3, 5]. The American Conference of Governmental Industrial Hygienists (ACGIH) currently sets the Biological Exposure Index (BEI) at 5 micrograms/g creatinine for workers exposed to airborne cadmium[6] and the World Health Organization (WHO) proposed a health-based limit of 10 nmole/mmole creatinine (10 μg/g creatinine)[7]. There have been studies that do not agree that these limits are reasonable[8, 9] and it has been stated "it seems that there is a serious underestimation of the risk and an overestimate of the 'critical concentration' of cadmium in urine and the kidneys"[4].

Since the 1950s, exposure to cadmium in the working environment has improved remarkably, with concentrations of cadmium dust and fumes in factories decreasing to relatively low levels. Investigators report that factory levels in Sweden, in 1998, were typically at or below the existing Swedish occupational exposure limits of 0.05 and 0.01 mg/m^3 for total dusts and respirable dust, respectively[4]. ACGIH currently sets a TLV of 0.01 mg/m^3 for the inhalable fraction of cadmium dust[6].

Because the number of workers with high cadmium exposure is decreasing in developed countries, studies on the effects of high exposure to Cd are limited, but the present exposure of Chinese workers to Cd may be likened to that of factories in developed countries prior to the 1950s. This paper reports the findings of a cross-sectional study of renal damage in workers from a Chinese Ni-Cd battery factory between April and May 1998.

Subjects and Methods

The survey population was from Xinxiang battery factory founded in 1959 in Henan Province, in which nickel-cadmium batteries are the principal products. Jobs related to cadmium exposure included powder mixer operator, powder wrapper, punching machine operator, cathoder, dotwelder, assembler, administrator and repairer. The processes for the manufacture of Ni-Cd batteries are dependent upon the size of the battery, but the basic process consists of the preparation of the cadmium and nickel powders (powder mixer operator), plate making (powder wrapper, punching machine

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Correspondence to: G. Zhang, School of Public Health, Curtin University of Technology, GPO Box U1987, Perth WA 6845 Australia

Table 1. General information on survey population

Job title	Number	Male	Female	Age (year)			Years of exposure (YoE)		
				Mean	Range	Std deviation	Mean	Range	Std deviation
Powder mixer operator	5	5		36.0	27–47	9.3	16.0	10.5–28.0	7.1
Powder wrapper	23	22	1	30.2	23–52	8.3	8.4	1.0–28.0	6.0
Punching machine operator	24	20	4	34.0	26–53	8.4	12.7	1.0–30.0	8.5
Cathoder	54	15	39	33.0	19–53	6.7	10.5	1.0–37.0	6.4
Dot welder	46	33	13	29.3	21–49	5.7	8.6	1.0–22.5	5.2
Assembler	36	14	22	30.5	21–53	7.6	10.6	1.0–29.5	6.8
Administrator and repairer	23	19	4	32.6	17–53	10.1	11.6	1.0–30.0	8.9
Others	3	2	1	30.3	28–33	2.5	4.5	1.5–8.0	3.3
Total	214	130	84	31.7	17–53	7.8	10.3	1.0–37.0	6.9

operator, cathoder and dot welder), assembly (assembler) and the charging-discharging of the batteries.

The survey population consisted of 214 workers who were involved in the manufacture of large batteries and had worked in making the large cells for more than one year, and who did not have any clinical diseases and were not taking medicine in the last month. Cadmium exposure was generally high for these workers, and at the same time it is likely that the workers were exposed to varying levels of nickel.

The workers had urine and blood samples collected on their rest day. All glassware and plastic ware were soaked overnight in 30%(v/v) nitric acid, thoroughly rinsed with deionized water and dried. Analyses were carried out are as follows:

1. The urinary cadmium[10] (CdU) and whole blood cadmium[11] (CdB) concentrations were determined by graphite-furnace atomic-absorption spectrometry (ShimadzuAA-670): for urine cadmium, the detection limit was 0.28 μg/*l*, the linear range of calibration 0.0–40.0 μg/*l*, variation coefficients 1.2–4.6% and the recovery rates were 96.4–100.7%. CdB quality control was ensured by using a standard blood sample from the Institute of Occupational Medicine of the Chinese Academy of Preventive Medicine in Beijing; where the detection limit was 0.66 μg/*l*, the linear range of calibration 2.0–32.0 μg/*l*, variation coefficients 4.4–10.7%, and recovery rates for blood cadmium 96.8–106.8%.

2. Urine creatinine was measured by a routine colorimetric procedure.

3. For B-microglobin (B_2-MG) measurements, a radioimmunoassay procedure[12] (provided by Beijing Biological Manufacture Factory, batch number 95:R-25) was used. The workers were asked to empty their bladders and drink some water, then fresh urine samples were collected and tested for pH by using pH testing strips: if the pH was less than 5.5 the urine samples were discarded.

3. After preservation by freezing, urine retinol-binding protein (RBP) was measured by radioimmunoassay at the Institute of Occupational Medicine of the Chinese Academy of Preventive Medicine.

4. Urine albumin protein (AP) was measured by a radioimmunoassay procedure (provided by Beijing Biological Manufacture Factory, batch number 94:F-11).

All the statistical analyses were performed with SPSS 8.0.

Results and Discussion

The concentration of cadmium in the working area is based on area sampling of the large battery manufacturing area between 1986 and 1992, giving the geometric mean of the cadmium concentration in CdO dust as 2.17 mg/m^3 (approximately 200 times the current TLV[6] with a range 0.1 to 32.8 mg/m^3. Of the 214 exposed workers, 10 had more than 100 μg/g cr of CdU, which is similar to the results from a European country in the 1950s[13]. The job titles, age, sex and working period were recorded for the surveyed workers (Table 1).

In a cross-sectional study the time of exposure may be estimated from the years of exposure, therefore, in this study the years of exposure (YoE) was used as an indicator of total exposure. Figure 1 shows the relationship between CdU and years of exposure in the workers. It can be seen that the CdU level of workers with >15 yr of exposure, with an average age of 42, is lower than for those with 10 to 15 yr of exposure, implying no apparent correlation between CdU and years of exposure in the long exposure group. In general it has been accepted that in the absence of renal damage, the measurement of cadmium in urine reflects the body-burden of cadmium[4]. As a result, a lack of correlation between CdU and years of exposure in the long exposure group may be attributed to renal damage in that group. To explore this issue further, the 14 workers who had a B_2-MG of more than 1000 μg/g cr were discarded, because in China this level is taken as evidence of renal damage[14]. The relationship between CdU and years of exposure in the remaining

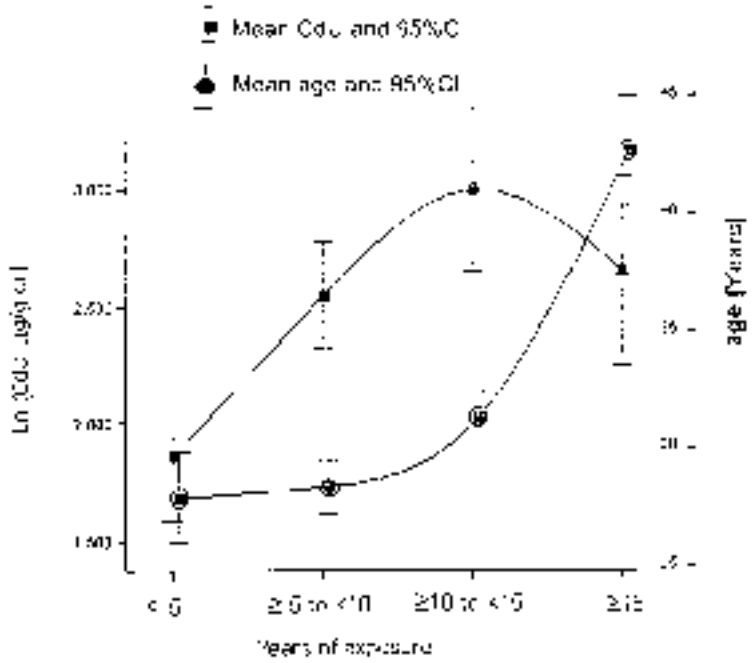

Fig. 1. Trends of urine cadmium with age and years of exposure in 214 workers.

200 workers is shown in Fig. 2. It can be seen that in the group with more than 15 yr exposure the urinary cadmium decreases and the mean age increases sharply, i.e. in the older exposed workers the urinary cadmium does not increase sharply with the years of exposure. No significant difference between Fig. 1 and Fig. 2 is found, the correlation coefficients between CdU and years of exposure before discarding and after discarding are 0.218 and 0.211, respectively. These data indicate that discarding the workers who have renal damage does not change the correlation, implying that renal damage is not the cause of lower CdU values in workers with >15 yr exposure. This result agrees with a report on a non-occupationally exposed population, where urinary cadmium did not increase with age after people reached 30 yr of age[13].

Urine and blood Cd levels have been tabulated with respect to the workers' job title (Table 2). In general it can be seen that increased CdU and CdB levels are associated increased B_2-MG, RBP and AP levels, i.e. high Cd levels are associated with renal damage. An exception to this exists for the powder mixer operators, in which the concentrations of CdU and CdB are amongst the lowest whilst levels of B_2-MG, RBP and AP are the highest, indicating renal damage. The finding stated earlier, that urinary cadmium does not increase sharply with the years of exposure in the older exposed workers, may explain the exception because this group of workers generally had the highest age and years of exposure. Because, as the hygiene survey information suggests, the job of the power mixer operators was to prepare cadmium powder as well as nickel powder whether the exception is related to special job activities or not needs to be studied further.

Bivariate correlation coefficients and partial correlation coefficients (controlling for gender and urine pH) between years of exposure and biological parameters have been calculated (Tables 3 and 4, respectively). The results show that there is a correlation between CdU and years of exposure (bivariate correlation coefficients and partial correlation coefficients were more than 0.2 and $P<0.01$) in these high exposure workers, but no correlation is found between blood cadmium levels and exposure, supporting the claim that urinary cadmium reflects the amount of body burden and blood cadmium is related to recent exposure[4]. As expected, a stronger correlation is seen between those parameters that reflect similar clinical significance, such as CdU and CdB or B_2-MG and RBP.

Workers were categorized according to their levels of CdU and CdB, and their renal protein excretion geometric mean calculated (Tables 5 and 6, respectively). It can be seen that as levels of CdU and CdB increase, concentrations of B_2-MG, RBP and AP also increase (there is significant difference in renal protein excretion for CdU and CdB levels, except for RBP in CdU levels). The results indicate that CdU and CdB are significant as cadmium exposure indicators.

Some studies suggest that a urinary cadmium

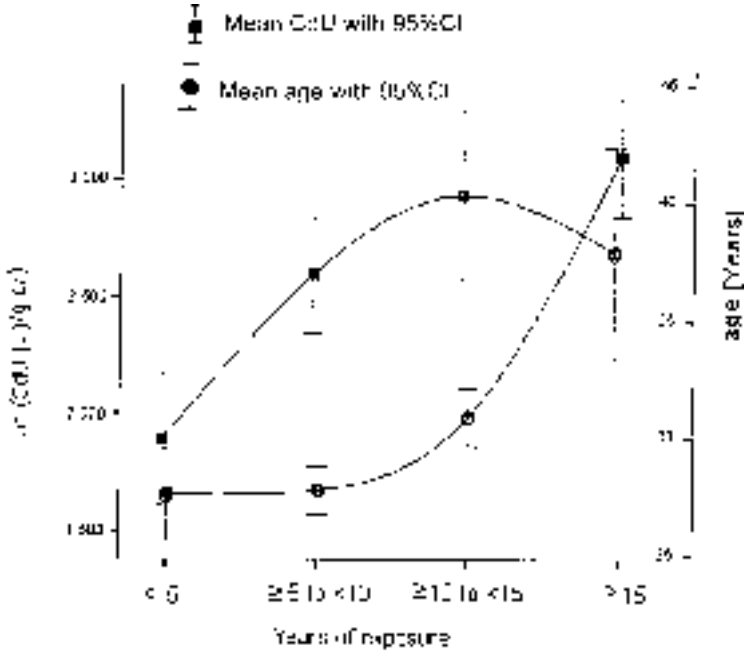

Fig. 2. Trends of urine cadmium with age and years of exposure in the 200 workers with less than 1000 μg/gcr of urine B_2-MG.

Table 2. Biological parameters of different job titles

Job title	Number	CdU (ug/gcr)		CdB (ug/*l*)		B_2-mg (ug/gcr)		RBP (ug/gcr)		Ap (ug/gcr)	
		GM	GSD	GM	GSD	GM	GSD	GM	GSD	GM	GSD
Powder mixer operator	5	4.0	1.7	8.7	2.1	597.6	2.5	316.2	2.7	15.0	1.7
Powder wrapper	23	21.4	4.1	17.4	2.3	389.1	3.8	72.5	2.9	13.6	2.4
Punching machine operator	24	10.9	3.1	10.0	1.9	247.1	2.6	87.4	3.1	6.0	3.7
Cathoder	54	14.1	3.0	8.9	2.6	177.4	3.3	41.1	3.2	7.6	3.2
Dot welder	46	18.9	2.9	12.3	2.8	226.7	3.7	52.4	3.2	4.4	2.6
Assembler	36	13.9	2.9	9.8	2.5	146.1	3.1	40.5	2.4	5.7	3.0
Administrator and repairer	23	4.2	1.7	3.8	2.5	146.1	2.8	28.3	2.8	4.2	3.0
Others	3	5.1	2.2	6.2	3.4	215.5	1.8	11.5	8.3	3.1	3.1
Total	214	12.8	3.2	9.5	2.7	206.5	3.3	49.5	3.3	6.3	3.1

GM: abbreviated from geometric mean. GSD: abbreviated from geometric standard deviation. The GSDs were the counter-logarithmic figures that were calculated from the logarithmic values of original data.

concentration of 10 μg/g cr would be a safe level, below which kidney damage would rarely develop[15, 16]. The ACGIH has set a BEI for CdU of 5 micrograms/g creatinine for workers exposed to cadmium, but the literature on the health effects of cadmium exposure was recently reviewed and the BEI of 5 micrograms/g cr was described as being "a serious underestimation of the risk and an overestimate of the "critical concentration" of cadmium in urine and the kidneys"[4]. With 460 μg/gcr of B_2-MG as the normal value[17], the percentages of renal tubular B_2-microglobulinuria in workers with different urinary cadmium levels were calculated (Fig. 3). It can be seen that urinary cadmium levels of 3 to 60 μg/g cr relate to between 15% and 19% of the workers having B_2-MG proteinura. Of the workers who had a urinary cadmium level of less than 3 μg/g cr, only one worker (5%) had a positive result for B_2-MG proteinuria. For the range of 3 to 5 μg/gcr CdU, our data show that the percentage of B_2-MG proteinuria in workers is approximately 15% (Fig. 3), which suggests that a urinary cadmium concentration of 5 μg/g cr may not be a safe level for the occupationally exposed population. This

Table 3. Bivariate correlation coefficients for biological parameters

	YoE	CdU	CdB	B2-MG	RBP	Ap
YoE	1					
CdU	.218**	1				
CdB	.133	.641**	1			
B2-MG	.137*	.346**	.324**	1		
RBP	.253**	.219**	.306**	.575**	1	
Ap	.085	.266**	.147	.419**	.400**	1

For CdU, CdB, B2-MG, RBP and Ap Ln value was used for correlation coefficients. *: P<0.05; **: P<0.01.

Table 4. Partial correlation coefficients for biological parameters

	YoE	CdU	CdB	B2-MG	RBP	Ap
YoE	1					
CdU	.226**	1				
CdB	.133	.677**	1			
B2-MG	.135*	.399**	.338**	1		
RBP	.254**	.270**	.312**	.545**	1	
Ap	.088	.257**	.183*	.430**	.421**	1

See notes on Table 3.

Table 5. One-way analysis of influence of different urine Cd Levels on protein excretion

	CdU<5 μg/gcr		CdU≥5 and Cdu<10 μg/gcr		CdU≥10 μg/gcr		F	P
	GM	GSD	GM	GSD	GM	GSD		
B2-MG (μg/g cr)	132.0	3.2	203.0	3.0	257.2	3.4	5.8	.003
RBP (μg/g cr)	37.3	3.7	50.4	2.8	56.3	3.2	2.2	.110
Ap	4.5	3.4	6.0	3.0	7.5	2.9	3.8	.023

GM and GSD see notes on Table 2. F: F ratio of ANOVA analysis. P: F Prob of ANVOA analysis.

Table 6. One-way analysis of influence of different blood Cd Levels on protein excretion

	CdB<5 μg/*l*		CdB≥5 and <10 μg/*l*		CdB≥10 μg/*l*		F	P
	GM	GSD	GM	GSD	GM	GSD		
B2-MG (μg/g cr)	140.6	3.0	151.1	3.4	296.7	3.2	10.4	.000
RBP	32.7	3.1	40.9	2.7	68.5	3.3	9.0	.000
Ap	5.5	2.9	4.6	3.4	7.7	3.0	4.1	.017

see notes on Table 5.

conclusion should be drawn with caution, because as Jarup and co-workers stated, "when persons with cadmium-induced tubular damage are examined a long time after the appearance of tubular dysfunction, the dose-response curve shifts to the left. For example, a 10% prevalence of B_2-MG proteinuria was seen at a urinary cadmium level of about 6.5 μg/gcr in 1984, as compared with 3.5 μg/gcr when the same group of workers were examined 10 years later"[4]. In the study reported here it was not possible to determine the presence or otherwise

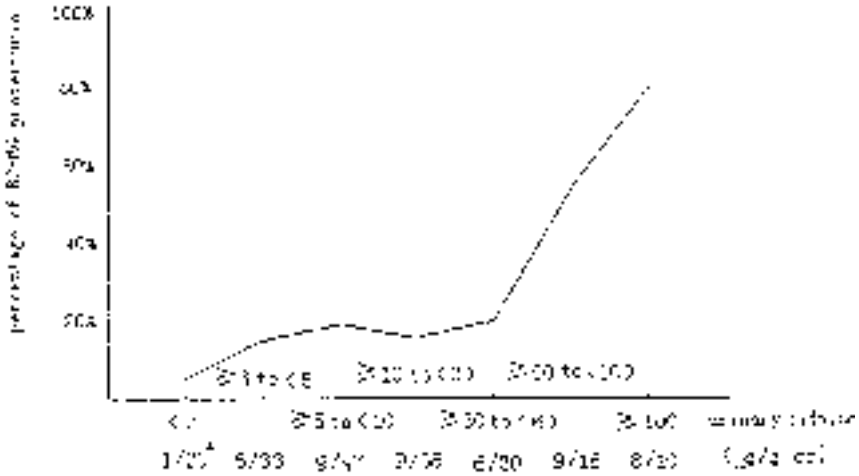

Fig. 3. Proportion of B_2-MG proteinuria by urine cadmium level**. *: number of B_2-MG proteinuria workers/total workers. **: trend test shows that the relationship between urinary cadmium and B_2-MG proteinuria is significant ($p<0.001$).

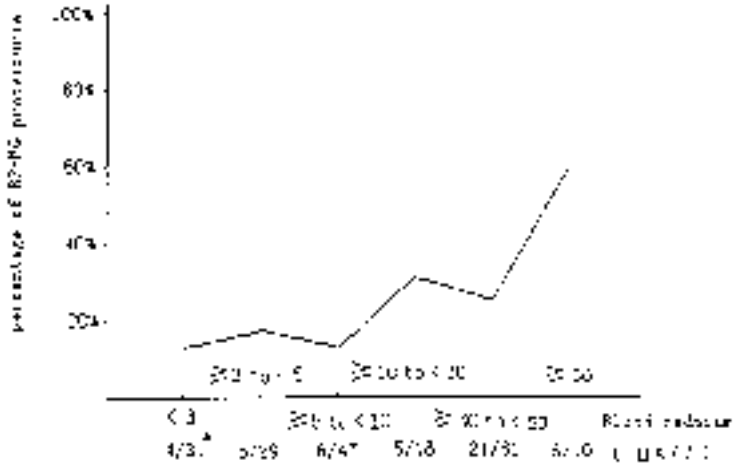

Fig. 4. Proportion of B_2-MG proteinuria by blood cadmium level. *: number of B_2-MG proteinuria workers/total workers. **: trend test shows that the relationship between blood cadmium and B_2-MG proteinuria is significant ($p<0.05$).

of a left-shift.

For blood cadmium, ACGIH has set a BEI of 5 $\mu g/l$ for workers exposed to cadmium[6]. With the normal value for B_2-MG mentioned above, the percentages of renal tubular B_2-microglobulinuria in workers with different blood cadmium levels were calculated (Fig. 4). Figure 4 indicates that for workers with CdB levels of 3 to 10 $\mu g/l$ the percentage of B_2-MG proteinuria was between 13 and 17%, for those with blood cadmium levels above 10 $\mu g/l$ the percentage of B-MG proteinura increased sharply. Below the CdB level of 3 $\mu g/l$, 4 workers (13%) had B_2-MG proteinura. It was not possible to find a minimum value of B_2-MG proteinuria for blood cadmium in this occupationally high exposure population because 3 $\mu g/l$ is too close to the 2 $\mu g/l$ (95thpercentiles) of CdB measured in the general population[18]. Nevertheless, the correlation between CdB and CdU or urine protein excretion was significant (Table 4), suggesting that blood cadmium could be considered as a biological index for cadmium exposure or renal damage.

Conclusion

This study indicates that urinary cadmium does not increase significantly with years of exposure in older workers exposed to cadmium, suggesting that the significance of urinary cadmium in older workers should

be explored further. For those workers with high cadmium exposure a urinary cadmium concentration of 5 μg/g cr or a blood cadmium concentration of 5 μg/*l* may not be a safe level because at this level it would be expected that more than 10% of the exposed population would experience B_2-MG proteinuria. Although urinary cadmium and blood cadmium may be considered as indicators of renal damage for exposed workers, it is difficult to set a health-based limit for those workers.

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