Short Communication

CHANGES OF BLOOD AND
URINARY LEVELS OF COBALT
DURING SINGLE EXPOSURE TO
COBALTコバルト 1 回曝露における血中および
尿中コバルト濃度の変化

Key words: cobalt exposure; blood; urine; biological half time; chelating resin

Cobalt widely used in modern industries is considered to cause various diseases such as interstitial lung disease, asthma, cardiomyopathy, and contact dermatitis.¹⁾ Previously, we reported that cobalt (Co) concentration in the urine (CoU) or blood (CoB) of a worker can be a good indicator of cobalt exposure.²⁾ However, the biological half time (BHT) of CoU or CoB under the condition of occupational exposure has not been established. We therefore performed a single-exposure study in a hard metal tool factory using healthy volunteers.

Materials and methods. a) Subjects: Seven healthy male volunteers (aged 23.1 ± 1.1 yr) with no previous history of exposure to Co were asked to sit for 6 h (13:00–19:00) at the work site in a hard metal tool factory where workers shape semisintered tool materials. Each volunteer monitored the dust concentration with an optical dust indicator (P-3, Shibata) at his sitting place every 5 min throughout the exposure period and the level of the Co exposure was measured as described previously.³⁾ b) CoB measurement: Blood sampling was made at 0 and 6 h from the start of exposure. Five grams of blood was freeze-dried (FD-5, Rabconco) for 36 h and ashed for 48 h with a low temperature asher (LTA-152, Yanagimoto), and ashing was completed using 3 ml of HNO_3 . To eliminate iron (Fe), alkali and alkaline earth elements, Chelex-100 (100–200 mesh, Bio Rad Lab.) was used. The ashed sample was dissolved in 1 ml of 2 N HCl and adjusted to pH 5–5.5, to which 0.5 ml of 8 M ammonium acetate (pH 5.3) and 2 ml of 1 M ammonium acetate-0.25 M pyrophosphate (pH 5.3) were added and the mixture was pipetted onto 2 ml of Chelex-100 column. The procedure of cleaning of the sample was the same as that reported by Marino and

Table 1. Recovery of cobalt after its addition to 5 g of blood.

N	Cobalt added $\mu\text{g/dl}$	Mean $\pm$ S.D. $\mu\text{g/dl}$	Coefficient of variation %	Recovery rate %
9	+ 0	0.043 ± 0.004	9.3	—
9	0.043 ± 0.15	0.201 ± 0.017	8.5	103.1
9	0.043 ± 0.73	0.780 ± 0.025	3.2	100.9

0.043 $\mu\text{g/dl}$ is the original concentration of cobalt in blood.

Ingle.³⁾ The effluents were collected in a 20-ml beaker and heated to dryness on a hot plate at 150°C . The residue was dissolved in 0.5 ml of 0.1 N HNO_3 and analyzed for Co with a Hitachi 170-70 Zeeman-effect electrothermal atomic absorption spectrophotometer under the conditions described previously.²⁾ The detection limit for Co in 0.1 N HNO_3 solution was 1 ng/ml at a signal level equivalent to twice the noise level and that for CoB was calculated to be $0.01 \mu\text{g}/100 \text{ g}$ when 5 g of blood was used. As shown in Table 1, recovery of Co was found to be 100%. The elimination of Fe and calcium (Ca) from the blood samples ($N=9$) was found to be almost complete because the concentrations of Fe and Ca in 0.5 ml of 0.1 N HNO_3 with 5 g of blood were 1.5 ± 0.3 and $3.0 \pm 0.2 \mu\text{g/ml}$, respectively. c) CoU measurement: Urine sample was obtained at 0, 4, 6, 24, 30, 48 and 72 h from the start of exposure and all the other urine specimens excreted during 0–24 h were also collected separately. CoU was determined as described previously.³⁾ The biological half time (BHT) of CoU(T) was calculated by the formula $y = ae^{-(\ln 2/T)t}$, using a method of least squares, where (y) is CoU at (t) h after the start of exposure.

Results and discussion. The mean Co concentration in the breathing zones of the seven volunteers was $19.4 \pm 5.5 \mu\text{g}/\text{m}^3$ ($10\text{--}28 \mu\text{g}/\text{m}^3$). The variation coefficient of the dust indicator value was 11–23% during each exposure and the Co content of the hard metal dust was $3 \pm 1\%$. The results showed that the volunteers had an almost constant Co exposure throughout the experiment. The mean CoB was $0.07 \pm 0.04 \mu\text{g/dl}$ ($0.03\text{--}0.16 \mu\text{g/dl}$) at the start and $0.11 \pm 0.05 \mu\text{g/dl}$ ($0.04\text{--}0.19 \mu\text{g/dl}$) at the end of the 6-h exposure. There was no statistically significant difference between these levels and both were within the normal range.¹⁾ The mean CoU during and after exposure is given in Table 2. An evident decrease

Table 2. Mean cobalt concentration in urine during and after single exposure.

Hours from start of exposure	Cobalt concentrations in urine		
	Unadjusted μg/l	Adjusted to S.G. at 1.024 μg/l	Adjusted to creatinine μg/g
0	2.2 ± 1.4 (0.5-4.8)	2.1 ± 0.9 (0.7-3.2)	2.1 ± 1.4 (N=6) (0.5-4.6)
4	5.3 ± 2.8 * (1.7-9.5)	6.5 ± 2.9 * (3.0-10.0)	5.1 ± 1.6 * (2.8-7.6)
6	8.5 ± 4.2 * (3.6-15.3)	11.9 ± 4.4 * (5.6-14)	11.0 ± 6.9 * (3.4-25)
11	7.3 ± 3.5 * (3.4-12)	9.3 ± 5.3 * (3.9-19)	6.4 ± 3.6 * (2.7-11.5)
20	4.6 ± 1.2 * (2.5-6.0)	5.7 ± 3.2 * (2.3-10.3)	3.3 ± 1.9 (1.2-6.6)
24	3.6 ± 2.1 (0.6-6)	4.5 ± 3.0 (1.1-9)	3.4 ± 2.2 (0.6-7)
30	2.9 ± 1.6 (0.8-5.0)	4.0 ± 2.0 (1.5-6.0)	2.7 ± 1.3 (1.3-4.0)
48	1.9 ± 1.1 (0.5-3.7)	2.2 ± 1.1 (0.9-4.0)	1.2 ± 0.4 (0.6-1.8)
72	2.1 ± 1.9 (0.5-5.7)	2.1 ± 1.5 (0.5-4.4)	1.0 ± 0.6 (0.3-1.8)

* : When value is compared with that at 0 hour, the difference is statistically significant (P > 0.05).

of CoU after cessation of exposure has been observed in highly exposed workers,^{4,5)} but, in single exposure, in spite of low exposure level, a significant change is observed as shown in Fig. 1. Since it was reported that injected Co was mainly excreted from urine^{6,7)} and about 90% of absorbed Co was decreased with 0.3-1 d of BHT,^{7,8)} an evident change was observed in CoU. In this study BHT of CoU are estimated to be 15.4 h for unadjusted value, 14.9 h with specific gravity at 1.024, and 11.8 h with creatinine adjustment. It was reported that a clearance of inhaled or intravenously/orally injected Co-60 to men showed three components of BHTs, 0.3-1 d, 3 d, and 60 d,^{7,8)} and our BHT agreed with that of the initial phase. These results suggest that a large part of absorbed Co is rapidly excreted from urine. Therefore, the time of urinary sampling should be carefully considered when CoU is used as an exposure indicator.

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Fig. 1. Urinary excretion patterns of cobalt during and after single exposure. ○ unadjusted value; ◐, adjusted to specific gravity at 1.024; ●, adjusted to creatinine. ■, exposure duration.

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