# Personal indium exposure concentration in respirable dusts and serum indium level

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**Abstract:** The aim of this study was to assess the relationship between indium exposure concentration in the respirable dust fraction (In-E) and indium in serum (In-S) in workers. Methods: A total of 39 workers were studied. The study subjects were categorized into 3 groups, namely, smelting workers (n=7), ITO workers (n=6) in an ITO grinding plant, and other workers (n=26). In-E and In-S ranged from $0.004-24.0$ $\mu$g/m$^3$ and $0.1-8.50$ $\mu$g/L, respectively. The simple regression equation was log(In-S)=$0.322 \times$log(In-E)$-0.443$. The simple correlation coefficients for the smelting workers, ITO workers and other workers were 0.489, 0.812 and 0.163, respectively. The differences in the relationships among the three groups suggest that In-S may vary with the chemical form to which the workers were exposed. In-E and In-S seem to be positively correlated. The correlation coefficient was higher for both smelting and ITO workers than for other workers.

**Key words:** Indium, Biological monitoring, Indium in serum, Smelting worker, Indium-tin oxide target plate (ITO), Personal respirable dust

Recent epidemiological studies in Japan revealed that the inhalation of hardly soluble indium compounds causes interstitial and emphysematous lung diseases[1–4]. Based on the dose-effect and dose-response relationships between indium in serum (In-S) and Krebs von den Lungen-6 (KL-6), the Japan Society for Occupational Health (JSOH) recommended an occupational exposure limit based on the biological monitoring (OEL-B) of indium of 3 $\mu$g/L of In-S in 2007. However, no information is available regarding the relationships between indium exposure and its biological exposure or effect indices.

In 2013 and 2014, we performed cross-sectional studies in 10 indium metal processing plants and 1 indium-tin oxide target plate (ITO) grinding plant where the external and internal exposure indices of indium were expected to be correlated, and measured the 8-hour time-weighted average (8h-TWA) exposure concentrations of indium in the respirable dust fraction (In-E, $\mu$g/m$^3$) and of indium in serum (In-S, $\mu$g/L). The aim of this study was to assess the relationship between In-E and In-S.

This study was approved by the Ethical Committee, School of Medicine, Keio University (approval number 20110268), and written informed consent was obtained from all study subjects.

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In the 10 indium metal processing plants, the In-E was measured in the study of work-environment assessment conducted by the Japan Industrial Safety and Health Association and commissioned by the Ministry of Health, Labour and Welfare. In the ITO grinding plant, our research team measured the In-E.

The respirable fraction of dust in the breathing zone was collected using a respirable dust cyclone (GS-3, SKC Inc) at a flow rate of 2.75 L/min or a TR sampler (PM4 NWPS-254, Sibata Scientific Technology Ltd.) coupled with a minipump (MP-Σ3, Sibata Scientific Technology Ltd.) at a flow rate of 2 L/min. Because sampling times ranged from 251 to 483 min, we converted the concentration to a conventional 8h-TWA. In-E was measured using inductively coupled plasma mass spectrometry (ICP-MS) at the Kyushu University Center of Advanced Instrumental Analysis[2] or at the Japan Industrial Safety and Health Association[2, 5, 6].

All In-S values were measured by our research team using ICP-MS at the Kyushu University Center of Advanced Instrumental Analysis[2]. Detection limit of In-S was 0.1 $\mu$g/L.

The number of currently indium-exposed workers in whom both In-E and In-S were measured was 64. Among the 64 workers, 23 were excluded from the analysis because their In-S levels were less than the detection limit (<0.1 $\mu$g/L). These 23 workers were categorized dental technicians (n=9), workers of bonding (n=1), solder manufacturing (n=10) and other indium metal processing (n=3). One worker with an occupational history of ITO manufacturing from several years prior and one worker with practically no exposure as of the sampling day (In-E: 0.00002 $\mu$g/m³) were also excluded. Ultimately, the study subjects included 39 workers. The study subjects were categorized into three occupational groups, namely, ITO grinding workers (n=6, ITO workers), workers in indium alloy smelting plants using high-temperature furnaces ($\geq$1000°C) (n=7, smelting workers), and dental technicians and workers of bonding, solder manufacturing and other indium metal processing (n=26, other workers).

*Statistical analysis*

To compare In-S and In-E among the three groups, the values were log-normally transformed to an approximately normal distribution before analysis, the geometric means (GM) and the geometric standard deviations (GSD) were calculated, and the Steel rank sum test was applied. A single regression model and a single correlation analysis were used to evaluate the relationship between In-E and In-S.

Statistical significance was assessed with $p<0.05$. All statistical analyses were performed using JMP version 11.0.0 (SAS Institute).

The mean age of the subjects was 38.5 years (range 20–63), 87.5% were male, and 47.5% were current smokers. The mean duration of indium exposure was 8.2 years (range 0.7–34.7).

In-E ranged from 0.004 to 24.0 $\mu$g/m³, and In-S ranged from 0.1 to 8.5 $\mu$g/L. The GM (GSD) of In-E was 0.97 (8.68) in the smelting workers, 1.22 (2.19) in the ITO workers and, 0.10 (6.49) in the other workers, respectively. The In-E values of the smelting workers and the ITO workers were marginally ($p=0.0709$) and significantly ($p=0.0069$) higher than the In-E values of the other workers. The GM (GSD) of In-S was 0.93 (4.50) in the smelting workers, 0.58 (3.26) in the ITO workers, and 0.12 (1.62) in the other workers, respectively. The In-S values of the smelting workers and the ITO workers were significantly ($p=0.011$ and $0.022$, respectively) higher than those of the other workers.

Figure 1a shows a scattergram of log(In-E) and log(In-S). The simple regression equation was log(In-S)$=0.322 \times$ log(In-E)$-0.443$, the regression coefficient was statistically significant ($p=0.0002$), and the simple correlation coefficient was 0.555 (95%CI 0.290–0.741).

Because the distribution of the In-E and In-S values was different among the three groups, scattergrams were displayed for each group (Figs. 1b, 1c, 1d). The simple correlation coefficients were 0.489 (95%CI −0.417–0.908) in the smelting workers (Fig. 1b), 0.812 (0.002–0.979) in the ITO workers (Fig. 1c), and 0.163 (−0.240–0.518) in the other workers (Fig. 1d). Due to the small number of subjects, the distributions of the In-E and In-S values in the smelting and ITO workers were not statistically significant, but they seemed to be linear (Fig. 1b, 1c).

As far as we know, this is the first paper concerning the relationship between In-E and In-S. Our research team has been interested in the relationship between In-E and In-S for a long time. However, we believed that it would be difficult to clarify this relationship because we believed that In-S may strongly reflect the amount of indium load in the lungs and, thus, the current In-S would not correlate to the current In-E. The reasons are supposed as follows: (1) due to the hardly soluble characteristics of indium compounds, the clearance rate of accumulated indium compounds in the lungs is very small[7]; (2) the In-S levels of formerly indium-exposed workers do not readily decrease[4] and the biological half-life of In-S in formerly exposed workers who perfectly removed from indium exposure is around 8
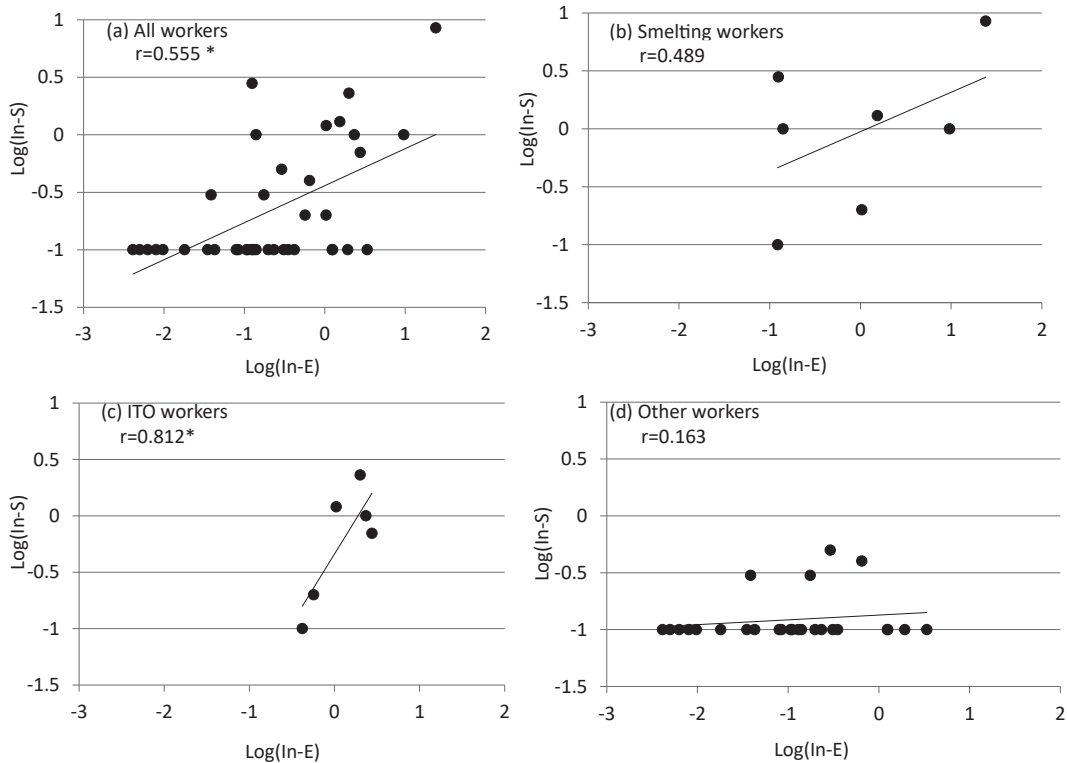
**Fig. 1.    Scattergram of log(In-E) and log(In-S) classified by job types.**
The x-axis represents log(In-E) and the y-axis represents log(In-S).
r: simple correlation coefficient. *: $p<0.05$.

years[8]; and (3) many indium processing plants have instituted labor hygiene management systems, and In-E and indium inhalation concentration may not be parallel due to the wearing of effective protective devices[6].

In this study, we had a chance to measure In-S and In-E in 11 plants that had not yet taken action to improve the work environment. Workers in these plants wore no or ineffective respiratory protective devices, and the In-E levels were expected to be low, so the indium load in the lungs of the workers could be expected to be small. However, it should be noted that extrapolation of this study's results to other indium-exposed populations requires careful consideration of whether the indium lung load in the population is actually negligible and whether the population wears appropriate respiratory protective devices.

After the log transformation of In-S and In-E, a significant positive correlation was observed (Fig. 1a). This suggests that In-S may increase In-E-concentration-dependently in the workers in this study.

Figures 1b, 1c and 1d seem to suggest that the relationship between In-E and In-S may vary due to the chemical form of the indium compounds. ITO, indium trioxide, indium metal, or indium alloy was the major chemical form in the ITO workers, the smelting workers[9], and the other workers. Though the number of workers was very small, In-E was correlated to In-S in the ITO workers and in the smelting workers, but not in the other workers. We have no information about the difference in the kinetics of each chemical form in the lung, but indium metal or indium alloy may show different kinetics unlike ITO or indium trioxide.

This study has some limitations. First, the number of study subjects was not sufficiently large, and information of relatively high In-E levels was lacking. This may make it difficult to smoothly interpret the results, and indicates a need to expand the study. Secondary, day-to-day variations of In-S are considered to be negligible, but day-to-day variations of In-E cannot be ignored. We may need to measure In-E on multiple days.

In conclusion, In-E and In-S seem to be positively correlated, but more data are needed to draw final conclusions. Studies of the kinetics in the lungs of each indium chemical form are also necessary to elucidate the relationship between In-E and In-S.

## Acknowledgments

## Conflict of Interest

None of the authors has any conflict of interest to disclose.

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