

# Cross-Sectional Study of Blood Lead Effects on Iron Status in Korean Lead Workers

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**OBJECTIVE:** This study assessed the iron status of Korean male lead workers by measuring the dietary iron intake and biochemical indices, and tested the hypothesis that a high blood lead level is associated with impaired iron function, which results in higher prevalence of iron deficiency when the route of exposure is not the gastrointestinal tract.

**METHODS:** One hundred eighteen lead workers and 42 non-lead workers were recruited from mandatory annual health surveillance sites for industrial workers. Blood lead, hemoglobin, and hematocrit levels were evaluated as hematologic parameters, and serum iron concentrations, total iron-binding capacity, and percentage of transferrin saturation were evaluated as iron-status parameters. Dietary iron intake was assessed by a 24-h recall method.

**RESULTS:** Lead workers had significantly lower hemoglobin, hematocrit, serum iron levels, percentage of transferrin saturation, and dietary iron intake than did non-lead workers, and they had significantly higher ( $P < 0.01$ ) total iron-binding capacity. The occurrence of iron-deficiency cases, as assessed by hematocrit values, was significantly higher ( $P < 0.001$ ) in lead workers than in non-lead workers, and the prevalence of iron deficiency was associated with high blood lead levels ( $P = 0.033$ ). The dietary iron intake was inversely associated with zinc protoporphyrin ( $P = 0.032$ ).

**CONCLUSIONS:** This study confirmed the adverse effects of high blood lead levels on hematologic pathways and the effectiveness of dietary iron intake as a secondary preventive intervention against lead toxicity. To promote health and to prevent toxic effects of lead exposure in Korean lead workers, an adequate intake of dietary iron is strongly recommended. *Nutrition* 2003;19:571–576. ©Elsevier Inc. 2003

**KEY WORDS:** iron status, dietary iron, blood lead, lead workers

## INTRODUCTION

Iron-deficiency anemia is one of the most prevalent nutritional concerns in developing and industrialized countries. The iron status of industrial workers occupationally exposed to lead is particularly important because a substantial body of evidence supports that iron deficiency not only impairs work performance<sup>1</sup> but also may increase the absorption and biotoxicity of lead in animals<sup>2–4</sup> and humans.<sup>5,6</sup> However, clinical investigations of gastrointestinal (GI) absorption of lead in adults has produced inconsistent results.<sup>5–7</sup> Intensive reviews on this topic can be found elsewhere,<sup>8,9</sup> but those works focused on iron and lead absorption through the GI tract, whereas the occupational exposures are mainly through the respiratory tract in the form of dust, vapor, or aerosol.<sup>10</sup> It is not clear, therefore, whether the evident beneficial effects of iron observed in studies of oral lead exposures would be the same in those cases in which lead exposure occurs through the respiratory tract.

Regular medical surveillance by annual health examinations and biological monitoring for the lead workers in Korea have shown that the number of lead-poisoning cases has decreased during the past two decades.<sup>11</sup> Despite these declines, there is considerable concern regarding the toxicologic implications of prolonged lead exposure and the subtle health effects at marginal blood lead (PbB) levels with deficits in anemia. Recent epidemi-

ologic studies reported more severe lead toxicity with impaired iron status for environmental lead exposure in children.<sup>12–14</sup> However, the results from the few studies involving adult men are inconsistent.<sup>12,15</sup> Although there is considerable support for the importance of adequate dietary iron intake in young children, there is little information regarding effects of dietary iron on lead absorption and on changing tissue levels of lead when adults are occupationally or environmentally exposed to lead through a route of exposure other than the GI tract. It is obvious that age greatly influences the accumulation of lead, so direct extrapolation of data from studies with infants or young children into occupational lead exposure of adults should be conducted cautiously.

The main objective of this study was to evaluate the iron status of the Korean lead workers by assessing dietary iron intake and hematologic and iron-status parameters. We conducted additional data analyses to ascertain whether increased PbB concentrations due to occupational lead exposures caused modifications of iron nutrition status, and whether modification of dietary iron intake can be used as an efficient secondary preventive intervention for occupational lead exposures when the exposure route is not through the GI tract.

## MATERIALS AND METHODS

### Study Population

One hundred thirty-five lead workers were recruited from two lead storage-battery factories. Among them, 118 male workers who had been provided with a periodical health surveillance program, in-

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cluding environmental and biological monitoring by the Institute of Industrial Medicine at Soonchunhyang University, Chunan, Korea, and without evident medical problems, were considered eligible for the present study: they participated in two site-visit examinations during September 2000. One hundred control subjects without occupational lead exposure were recruited from among non-lead-using industry workers who visited Soonchunhyang University Hospital for a mandatory annual medical examination between September and November 2000. We included only male workers due to very low ratio of female workers in Korean lead industries (average, 12.8%).<sup>16</sup> After a health screening examination, 42 eligible male subjects were selected to participate in the study as the non-lead-exposed control. We excluded 34 women and those who had been diagnosed with anemia, GI tract disease, hypertension, diabetes mellitus, liver or lung problems and those taking prescription drugs. Participation in the study was voluntary, and all participants provided written informed consent.

### Data Collection and Analysis

Information about medical history, demographic characteristics, and cigarette-smoking and alcohol-drinking habits was obtained and reviewed by an occupational physician. Dietary iron intake assessment was conducted by using a 24-h recall method by one-to-one interview with trained interviewers. Detailed descriptions of all foods and beverages consumed and estimated food portion sizes were recorded by trained interviewers using food models, standard household measures, and natural-size color photographs as memory aids. Food records were converted to nutrient intake by using a computerized nutrient analysis program (CAN-pro, Korean Society of Nutrition, Seoul, Korea). After height and weight were measured, percentage of body fat was measured by a portable bioelectrical impedance analyzer (TBF-501, Tanita, Tokyo, Japan) while the subject stood upright on a four-platform-type terminal impedance plethysmograph, in accordance with the manufacturer's instructions.

Approximately 10 mL of venous blood was collected and divided into two tubes: 4 mL of blood in a Vacutainer with ethylene-diamine-tetraacetic acid for hemoglobin (Hb), hematocrit (Hct), and PbB; and 6 mL of blood in a Vacutainer with SST Gel & Clot activator for serum iron (FeS) and total iron-binding capacity (TIBC). The level of zinc protoporphyrin (ZPP) was measured in a drop of fresh whole blood by using a portable hematofluorometer (model 206, Aviv, Lakewood, NJ, USA). PbB was analyzed at the Institute of Industrial Medicine, Soonchunhyang University (which is a certified reference laboratory for lead measurement in Korea) according to the Zeeman background-corrected flameless atomic absorption method by using a spectrometer with a graphite furnace (model Z-8100, Hitachi, Tokyo, Japan). Hb was assayed by the cyanmethemoglobin method (Sigma, St. Louis, MO, USA). FeS and TIBC were measured by a spectrophotometric procedure (TBA-40FR biochemical analyzer; Hitachi, Tokyo, Japan). Percentage of transferrin saturation (TS) was calculated by dividing FeS by TIBC and multiplying by 100. Quetelet's index [weight (kg)/height (m<sup>2</sup>)] was used as a measure of body mass index (BMI).

### Statistical Analysis

All statistical analyses were performed with SPSS 10.0. In exploratory data analysis, frequency distributions for continuous variables were used to identify and validate the outliers, and cross tabulations were conducted by categorical variables. Statistical significance was defined as  $P < 0.05$ . We used the chi-square test to compare frequency distributions. The difference between the means of lead and non-lead worker groups was assessed by Student's  $t$  test.

TABLE I.

GENERAL CHARACTERISTICS AND BLOOD LEAD LEVELS OF SUBJECTS			
	Non-lead workers*	Lead workers*	$t$
$n$	42	118	
Age (y)	42.88 ± 11.32	38.27 ± 10.23	2.323†
Height (cm)	169.33 ± 4.06	169.51 ± 6.18	-0.207
Weight (kg)	66.60 ± 8.51	65.71 ± 9.60	0.558
BMI (kg/m <sup>2</sup> )	23.52 ± 2.78	22.89 ± 3.24	0.627
Body fat (%)	24.63 ± 5.94	21.56 ± 5.25	2.829‡
Blood lead (μg/dL)	5.07 ± 1.34	30.88 ± 15.10	-17.977§
Smokers (%)	58	59	
Alcohol consumption (%)	82	74	

\* Values are mean ± standard deviation.

†  $P < 0.05$ .

‡  $P < 0.01$ .

§  $P < 0.001$ .

BMI, body mass index

To minimize extraneous errors in estimating dietary iron intake due to individual differences in total food intake, iron intake was adjusted for total energy intake. The calorie-adjusted iron intake for each individual was computed by taking the residual from the regression model in which total caloric intake was the independent variable and the observed iron intake was the dependent variable, plus a constant equal to the expected intake of iron for the mean caloric intake of the study population.<sup>17</sup>

Pearson's correlation coefficients were computed to explore the significance of relationships among covariates. Matrix scatter plots were developed from hematologic parameters and from ZPP values versus energy-adjusted dietary iron intake. We plotted ZPP values on a logarithmic scale to account for the skewness of the ZPP distribution. The potential effect of modification of the PbB on the relationship between dietary iron intake and hematologic parameters or log ZPP were examined with a linear regression model by forming two groups differentiated on the basis of PbB level: high-PbB (PbB ≥ 25 μg/dL) and low-PbB (PbB < 25 μg/dL). The fitted model was qualitatively tested for the assumptions of linear regression. Logistic regression was used to examine the relation between PbB levels (as categorized by group) and incidence of impaired hematologic parameter (Hct < 41%). Multivariate models were controlled for the effects of age, BMI, cigarette smoking, and alcohol consumption.

## RESULTS

Summary statistics of the subjects are shown in Table I. The lead workers were significantly younger than the non-lead workers ( $P < 0.05$ ). The non-lead and lead workers ranged in age from 24 to 79 y and from 20 to 65 y, respectively. Body fat percentages differed significantly ( $P < 0.01$ ) between groups, and PbB levels were significantly higher in the lead-worker group ( $P < 0.001$ ) than in the non-lead-worker group. There were more alcohol drinkers in the non-lead-worker group.

Table II shows the average values of hematologic parameters such as Hb and Hct, iron-status parameters including FeS, TIBC, and TS, and energy-adjusted dietary iron intake. Hb, Hct, FeS, and TS levels were significantly lower in the lead workers than in the non-lead workers, and TIBC was significantly higher ( $P < 0.01$ ) in the lead workers. All hematologic and iron-status parameters indicated that the iron status of the lead workers was lower than

TABLE II.

HEMATOLOGIC AND IRON-STATUS PARAMETERS AND DIETARY IRON INTAKE LEVELS OF SUBJECTS			
	Non-lead workers*	Lead workers*	<i>t</i>
Hematologic parameters			
Hemoglobin (g/dL)	15.07 ± 0.77	14.73 ± 1.09	2.217†
Hematocrit (%)	44.48 ± 2.47	41.92 ± 4.75	3.990§
Iron-status parameters			
Serum iron (μg/dL)	165.86 ± 52.35	124.21 ± 47.07	4.806§
TIBC (μg/dL)	309.36 ± 97.47	341.45 ± 47.98	-2.739‡
TS (%)	49.59 ± 16.93	37.08 ± 14.83	4.326§
Energy-adjusted dietary iron intake (mg/d)			
Iron from animal source	4.28 ± 2.85	4.10 ± 3.27	
Iron from plant source	10.28 ± 9.68	7.26 ± 5.42	

\* Values are mean ± standard deviation.

†  $P < 0.05$ .

‡  $P < 0.01$ .

§  $P < 0.001$ .

TIBC, total iron-binding capacity; TS, percentage of transferrin saturation

that of non-lead workers, although the mean values of all parameters were higher than the generally accepted lowest cutoff values.<sup>1,18</sup> A significantly lower ( $P < 0.05$ ) dietary iron intake was

observed in the lead workers than in the non-lead workers. Forty-five percent of non-lead workers and 66% of lead workers had dietary iron intakes lower than the level of the Korean recommended daily allowance, which is 12 mg/d for adult males. Although animal foods are generally considered to be better sources of iron than plant foods, due to better bioavailability, dietary iron intakes of lead workers and non-lead workers were mainly from plant foods such as legumes, fruits, cereals, and seaweed, as reported in elsewhere,<sup>16</sup> which reflects typical Korean dietary patterns.

Table III shows the iron status of subjects determined by different laboratory assessments of the relative body iron quantities of subjects according to the different stages of iron deficiency. Iron deficiency anemia was determined by using Hb concentration (<13.5 mg/dL), Hct (<41%), FeS (<40 μg/dL), TIBC (>410 μg/dL), or TS (<15%), as described by Gibson<sup>1</sup> and Lee and Nieman.<sup>18</sup> The second stage of iron deficiency, which is often referred to as iron-deficient erythropoiesis, was determined by FeS (<60 μg/dL), TIBC (>390 μg/dL), or TS (<15%).<sup>1,18</sup> Iron-deficiency anemia and iron-deficiency erythropoiesis were not high in either group. Thirteen percent of lead workers (according to Hb level) and 36% of lead workers (according to Hct) were found to be anemic, whereas significantly lower percentages of non-lead workers (0% and 7% according to Hb and Hct, respectively) were categorized as having iron-deficiency anemia. All iron-status parameters showed very low prevalence of iron-deficiency anemia in the lead and non-lead groups, in contrast to the results of Hb and Hct in the lead group. The iron-store depletion stage, which was characterized by FeS levels lower than 115 μg/dL, TIBC higher than 360 μg/dL, or TS lower than 30%,<sup>1,18</sup> was more prevalent in the lead group ( $P < 0.05$ ).

TABLE III.

IRON STATUS OF SUBJECTS AT DIFFERENT STAGES DETERMINED BY HEMATOLOGIC AND IRON-STATUS PARAMETERS				
		Non-lead workers, <i>n</i> (%)	Lead workers, <i>n</i> (%)	$\chi^2$
Iron-deficient anemia determined by hematologic parameters				
Hemoglobin (<13.5 mg/dL)	Yes	0 (0)	15 (13)	5.891
	No	42 (100)	103 (87)	$P = 0.012$
Hematocrit (<41%)	Yes	3 (7)	42 (36)	12.403
	No	39 (93)	76 (64)	$P < 0.001$
Iron-deficient anemia determined by iron-status parameters				
Serum iron (<40 μg/dL)	Yes	0 (0)	0 (0)	—
	No	42 (100)	118 (100)	
TIBC (>410 μg/dL)	Yes	4 (10)	8 (7)	0.336
	No	38 (90)	110 (93)	
TS (<15%)	Yes	0 (0)	3 (3)	1.088
	No	42 (100)	115 (97)	
Iron-deficient erythropoiesis determined by iron-status parameters				
Serum iron (<60 μg/dL)	Yes	1 (2)	4 (3)	0.104
	No	41 (98)	114 (97)	
TIBC (>390 μg/dL)	Yes	6 (14)	16 (14)	0.014
	No	36 (86)	102 (86)	
TS (<15%)	Yes	0 (0)	3 (3)	1.088
	No	42 (100)	115 (97)	
Iron depletion determined by iron-status parameters				
Serum iron (<115 μg/dL)	Yes	9 (21)	49 (42)	5.414
	No	33 (79)	69 (59)	$P = 0.025$
TIBC (>360 μg/dL)	Yes	8 (19)	46 (39)	5.506
	No	34 (81)	72 (61)	$P = 0.022$
TS (<30%)	Yes	5 (12)	40 (34)	7.412
	No	37 (88)	78 (66)	$P = 0.004$

TIBC, total iron-binding capacity; TS, percentage of transferrin saturation

TABLE IV.

UNADJUSTED CORRELATIONS BETWEEN BLOOD LEAD LEVEL AND ANTHROPOMETRIC, BIOCHEMICAL, AND NUTRITIONAL VARIABLES*		
Variables	Correlation coefficient ( <i>r</i> )	<i>P</i>
Age	0.185	0.021
Percent body fat	-0.056	0.492
Body mass index	-0.042	0.601
Hemoglobin	-0.121	0.135
Hematocrit	-0.098	0.224
Serum iron	0.010	0.901
TIBC	0.111	0.168
TS	-0.024	0.763
Energy-adjusted dietary iron intake	-0.234	0.003

\* *n* = 160 subjects.

TIBC, total iron-binding capacity; TS, percentage of transferrin saturation

Table IV shows the unadjusted correlations of PbB with different variables. Age was significantly associated with PbB level, with a correlation coefficient of 0.185. Dietary iron intake level was negatively associated with PbB level ( $P < 0.01$ ).

Unadjusted and multivariate models showed that prevalence of high PbB ( $\geq 25 \mu\text{g/dL}$ ) was associated with prevalence of iron-deficiency anemia (Hct  $< 41\%$ ; Table V). Subjects with low PbB levels ( $< 25 \mu\text{g/dL}$ ) showed significantly higher dietary iron intake ( $P < 0.05$ ) and were 56.6% less likely (95% confidence interval, 6.6–79.7%) to have iron-deficiency anemia than were subjects

TABLE V.

RELATIVE PREVALENCE OF IRON DEFICIENCY (HEMATOCRIT  $< 41\%$ ) IN TWO GROUPS WITH DIFFERENT PbB LEVELS (*N* = 160)

	High PbB*	Low PbB†	<i>t</i>
Blood lead ( $\mu\text{g/dL}$ )	39.92 $\pm$ 12.69	12.21 $\pm$ 7.26	16.145¶
Hemoglobin (mg/dL)	14.72 $\pm$ 1.06	14.97 $\pm$ 1.03	-1.467
Hematocrit (%)	42.27 $\pm$ 4.26	43.06 $\pm$ 4.73	-1.089
Serum iron ( $\mu\text{g/dL}$ )	131.28 $\pm$ 53.27	133.01 $\pm$ 47.62	-0.211
TIBC ( $\mu\text{g/dL}$ )	343.35 $\pm$ 51.00	336.84 $\pm$ 43.27	0.844
TS (%)	39.00 $\pm$ 16.48	40.14 $\pm$ 15.40	-0.440
Dietary iron intake (mg/d)	10.63 $\pm$ 4.93	14.27 $\pm$ 13.26	-2.349¶
<i>n</i> subjects‡	69	86	$\chi^2 = 2.502$
<i>n</i> prevalent cases of iron deficiency (%)	24 (35)	20 (23)	$P = 0.081$
Unadjusted OR (95% CI)	1.00	0.568 (0.281–1.149)	0.116
Multivariate-adjusted OR (95% CI)§	1.00	0.435 (0.203–0.934)	0.033

\* PbB  $\geq 25 \mu\text{g/dL}$ . Data presented as mean  $\pm$  standard deviation.

† PbB  $< 25 \mu\text{g/dL}$ . Data presented as mean  $\pm$  standard deviation.

‡ Five cases are missing.

§ Adjusted for age, body mass index, smoking, and alcohol use.

¶  $P < 0.05$ .

¶¶  $P < 0.001$ .

CI, confidence interval; OR, odds ratio; PbB, blood lead; TIBC, total iron-binding capacity; TS, percentage of transferrin saturation

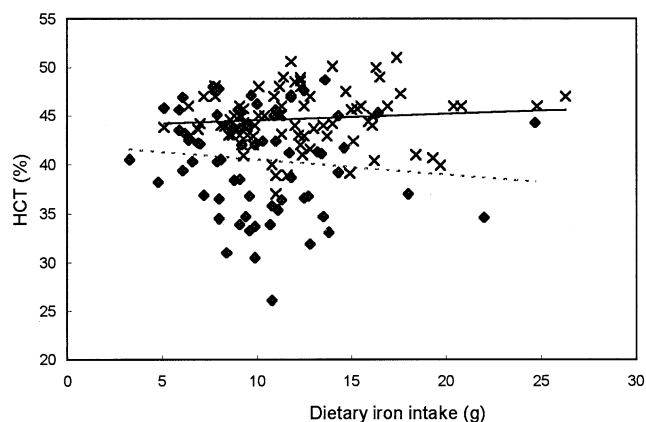


FIG. 1. Correlation between dietary iron intake and HCT values by blood lead levels demonstrated by linear regression lines. The dotted line represents high blood lead levels (diamonds, blood lead levels  $\geq 25 \mu\text{g/dL}$ ), with  $y = -0.30x + 45.39$  ( $R^2 = 0.066$ ,  $P = 0.034$ ). The solid line represents low blood lead levels ( $\times$ , blood lead levels  $< 25 \mu\text{g/dL}$ ), with  $y = 0.25x + 39.90$  ( $R^2 = 0.047$ ,  $P = 0.047$ ). HCT, hematocrit.

with high PbB, when adjusted with covariates known as possible confounders of PbB level, such as age, BMI, cigarette smoking, and alcohol drinking (multivariate trend,  $P = 0.033$ ).

A marginally significant, positive relation ( $\beta_{\text{low PbB}} = 0.257$ ,  $P = 0.047$ ) was found (by simple regression analysis) between dietary iron intake and Hct in the low-PbB group, whereas the relation was negative (and slightly more significant) in the high-PbB group ( $\beta_{\text{high PbB}} = -0.296$ ,  $P = 0.034$ ; Fig. 1). The difference between the slopes in the low-PbB and high-PbB groups was statistically significant ( $P < 0.05$ , data not shown). The regression results were robust to the inclusion of other explanatory variables, such as age, BMI, smoking, and alcohol drinking ( $\beta_{\text{low PbB}} = 0.127$ ,  $\beta_{\text{high PbB}} = -0.329$ ), and  $R^2$  values were slightly increased with the inclusion of other explanatory variables (0.133 for low PbB and 0.120 for high PbB). The regression results were not affected by groups containing lead and non-lead workers: the high PbB group included only lead workers, and, when the low PbB group was regressed only among the lead workers, the regression did not change (data not shown).

To determine the efficacy of dietary iron-intake modification as a secondary preventive intervention for lead toxicity, a scatter plot of dietary iron intake versus log ZPP was drawn according to the low- and high-PbB groups (Fig. 2). Because the ZPP value is often used as the parameter of the hematologic toxic consequences of lead<sup>19</sup> and due to the low PbB levels, the ZPP values of non-lead workers was not measured, and the data in Figure 2 include only lead workers. When possible confounding variables (age, BMI, smoking, and alcohol drinking) were controlled for, the multiple regression analysis revealed a weak relation between dietary iron intake and ZPP values for the low-PbB group ( $\beta_{\text{low PbB}} = -0.0035$ ,  $R^2_{\text{low PbB}} = 0.029$ ), whereas a significant ( $P = 0.032$ ) negative relation was observed in the high-PbB group ( $\beta_{\text{high PbB}} = -0.010$ ,  $R^2_{\text{high PbB}} = 0.319$ ).

## DISCUSSION

Among the subjects of the present study, the lead workers showed significantly lower iron status and lower dietary iron intake than did the non-lead workers. The lower iron status of lead workers could be attributable to higher PbB levels or lower dietary iron intake. Although many studies reported that low iron status causes a higher absorption of lead in the GI tract, resulting in higher PbB levels,<sup>2–6</sup> when lead was introduced through intraperitoneal injection to rats, no difference was reported in PbB levels between

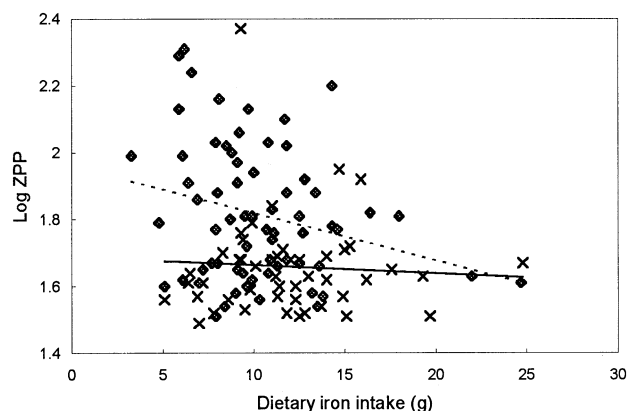


FIG. 2. Comparison of the correlation between dietary iron intake and log ZPP by blood lead levels illustrated by linear regression lines in the lead workers. The dotted line represents high blood lead levels (diamond, blood lead levels  $\geq 25 \mu\text{g/dL}$ ), with  $y = -0.0141x + 1.961$  ( $R^2 = 0.067$ ,  $P = 0.032$ ). The solid line represents low blood lead levels ( $\times$ , blood lead levels  $< 25 \mu\text{g/dL}$ ), with  $y = -0.0007x + 1.647$  ( $R^2 = 0.000$ ,  $P = 0.900$ ). ZPP, zinc protoporphyrin.

iron-adequate and iron-deficient groups.<sup>6</sup> Therefore, it would be unreasonable to expect that PbB was elevated due to the low iron status of lead workers, because the route of lead administration was mainly through the respiratory tract. The chances for GI exposures for this population are low because lead workers must comply to strict work practice regulations for lead industries in Korea to avoid unnecessary lead absorption other than through inhalation exposure due to undue high lead exposure in the workplace. The work practice regulations in the lead industries prohibits food or beverages in the workplace and requires proper wearing of a respirator, gloves, work clothes, mandatory shower after work, and changing into regular clothes.

Iron deficiency normally develops via successive stages, and each sequential event can be determined by various parameters, and a combination of such parameters is indicative of iron deficiency.<sup>1,18</sup> We measured two hematologic and three iron-status parameters. Gibson<sup>1</sup> and Lee and Nieman<sup>18</sup> described how values for the different tests change throughout the different stages of iron deficiency. Three successive stages of iron deficiency are explained by the amount of iron in three compartments (stores, circulating, and erythrocytes).<sup>18</sup> Although the first stage of iron depletion, in which iron stores are depleted but the amount of circulating and erythron iron is still sufficient, is reflected by decreased serum ferritin levels; serum ferritin was not analyzed in the present study. Our FeS, TIBC, and TS values revealed more subjects with depleted iron stores among the lead workers, whereas only a few subjects with iron-deficiency erythropoiesis were found in the lead and non-lead groups. Thus, we speculate that most subjects in this study had sufficient circulating iron, whereas 40% to 50% of lead workers and fewer than 10% of non-lead subjects had depleted iron stores. The third stage of iron depletion, iron-deficiency anemia with insufficient erythron iron, was not indicated by all parameters measured in this study. Surprisingly, more cases of iron-deficiency anemia were reported by hematologic parameters (Hb and Hct) than by iron-status parameters (FeS, TIBC, and TS) in the lead group, whereas results of the non-lead group were consistent between hematologic and iron-status parameters. High PbB would be a reasonable explanation for these results. High PbB would inhibit three major enzymes in heme biosynthesis,<sup>20</sup> and circulating iron could not be used efficiently for hematopoiesis because lead competes with iron for incorporation into erythrocytes.<sup>21</sup> In addition, lead would increase the rate of erythrocyte destruction,<sup>22</sup> shorten the erythrocyte life span,<sup>23</sup> and delay the regeneration of erythrocyte,<sup>24</sup> resulting in lowered he-

matologic parameters regardless of adequate erythron iron status of the lead workers.

Discrepancies between results of two hematologic parameters shown in Table III among the lead workers might be explained by the nature of the two parameters. Because Hct is the ratio of the volume of erythrocytes to the total volume of blood, its value may, unlike Hb, reflect all the hematologic enzyme inhibitory effects of lead, including the last step in the hematologic pathway and erythrocyte destruction. In addition, lead might interfere with heme synthesis in susceptible individuals, resulting in reduced function of the Hb protein and the erythrocyte, as indicated by reduced Hct in our study and by the small size of erythrocytes in another study<sup>14</sup> rather than by a quantitative reduction of Hb levels. This suggests that Hct is the better parameter to use in studies on hematologic lead effects, which is the reason we used it here.

There was a marginally significant relation between dietary iron intake and Hct. This may have relevance to the biosynthetic pathway of erythrocytes and different stages in development of iron deficiency. Hct or Hb values are the last parameters to be influenced by impaired iron status,<sup>1</sup> representing a long-term consequence of low dietary iron intake. The relation was negative (and slightly more significant) in the high-PbB group, which might lead to the interpretation that dietary iron absorbed by subjects with high PbB is not used as efficiently as those with low PbB and, as a consequence, results in their lower iron status. Therefore, the lower iron status observed in the lead workers might be the result of combined mechanisms of high PbB and low dietary iron intake. Our findings confirmed that high PbB changes iron use in the body, resulting in higher incidences of iron deficiency in subjects with high PbB. We also observed a significantly negative relation between ZPP levels, the parameter of hematologic toxic effect of lead,<sup>19</sup> and dietary iron. These results suggested that increasing the dietary iron intake might effectively modify the adverse health consequences of industrial lead exposure. This is further supported by the stronger relation between dietary iron intake and log ZPP value in the high-PbB group as opposed to the low-PbB group.

Caution must be used when interpreting the results of this current cross-sectional study, because they may have been subject to the following possible misclassification or measurement errors. First, a 24-h recall method is not a perfect tool for measuring dietary iron intake. Because we used a 1-d survey, menus on the study day may have falsely resulted in a low dietary iron intake of lead workers. Another potential measurement error might be expected due to the underreporting tendency of the 24-h recall method.<sup>25</sup> However, the probability of technical errors or information bias is not high in this study: most participants in the lead group and some in the non-lead group had participated in the meal plans provided by the company, so it is unlikely that the subjects had altered their diets. Moreover, we obtained the menus of the study day to check the accuracy of the subjects' memories. We also reduced measurement errors due to underreporting of dietary intake by taking energy-adjusted dietary iron intake values rather than crude intake values.<sup>17</sup> Although these measures may not have avoided all the problems associated with the 24-h recall method, it is unlikely that the associations we observed could be fully attributable to measurement error, because these measurement errors would generally bias the association toward the null.

Second, the cutoff value of  $25 \mu\text{g/dL}$  for high PbB was used, whereas in 1991 the U.S. Centers for Disease Control and the World Health Organization adopted  $10 \mu\text{g/dL}$  as the official action or guideline level of a maximum permissible PbB level of the general population. Our cutoff value was based on PbB levels that must exceed  $1.21 \mu\text{M/L}$  (equal to  $25 \mu\text{g/dL}$ ) before impaired hematopoiesis can be detected,<sup>13</sup> and the fact that the PbB levels of lead workers are higher than those of general population.

In conclusion, the present results suggested that adequate dietary intake of iron is essential for the promotion of health and the prevention of toxicity in industrial workers exposed to lead. As a

cross-sectional study, however, we cannot assert that dietary iron is an effective secondary preventive intervention because blood lead is a biomarker of lead accumulation over a certain period, and our data may not have properly provided information about dietary intake during the time of interest. Therefore, prospective studies should be conducted as soon as possible to better quantify the magnitude of the benefit. Moreover, it is clear from our data that many iron-sufficient lead workers still have high blood lead levels despite the decreasing number of lead-poisoning cases in Korea during the past two decades.<sup>11</sup> These results also suggested that additional lead exposure controls such as legislation and modern technology as the primary preventions are warranted in the lead industry.

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