

Changes in Systolic Blood Pressure Associated With Lead in Blood and Bone

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Background: Several studies have examined longitudinal associations of blood pressure change or hypertension incidence with lead concentration in blood or bone. It is not clear whether the observed associations reflect an immediate response to lead as a consequence of recent dose or rather are a persistent effect of cumulative dose over a lifetime.

Methods: We followed 575 subjects in a lead-exposed occupational cohort in South Korea between October 1997 and June 2001. We used generalized estimating equation models to evaluate blood pressure change between study visits in relation to tibia lead concentrations at each prior visit and concurrent changes in blood lead. The modeling strategy summarized the longitudinal association of blood pressure with cumulative lead dose or changes in recent lead dose.

Results: On average, participants were 41 years old at baseline and had worked 8.5 years in lead-exposed jobs. At baseline, the average \pm standard deviation for blood lead was 31.4 ± 14.2 $\mu\text{g/dL}$, and for tibia lead, it was 38.4 ± 42.9 $\mu\text{g/g}$ bone mineral. Change in systolic blood pressure during the study was associated with concurrent blood lead change, with an average annual increase of 0.9 (95% confidence interval = 0.1 to 1.6) mm Hg for every 10- $\mu\text{g/dL}$ increase in blood lead per year.

Conclusion: The findings in this relatively young population of current and former lead workers suggest that systolic blood pressure

responds to lead dose through acute pathways in addition to the effects of cumulative injury.

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Longitudinal change in systolic blood pressure is associated with lead measured in whole blood and bone. Previous studies of occupational or community cohorts reported that a one-time measurement of blood lead at baseline predicted future increases in systolic or diastolic blood pressure, but not all studies of lead and blood pressure have been consistent.^{1–6} Two of these studies also reported longitudinal associations with lead levels measured in patella or tibia bone compartments.^{1,5} The association of various lead dose measures with longitudinal change in blood pressure or hypertension incidence strengthens the body of evidence provided by many cross-sectional studies that lead may have a biologic role. It is not clear, however, whether the lead-associated elevations in blood pressure reflect an immediate response to lead at the biochemical site of action as a consequence of recent dose or rather are a persistent effect of cumulative dose over a lifetime.

Blood lead is a measure of recent lead exposure and reflects the balance among lead absorption, lead excretion, and storage and release from bone and soft tissue.⁷ Bone lead concentration, particularly in cortical bone from which the clearance half-life is 1 to 4 decades,^{8,9} is considered to be the best cumulative measure of past lead exposure.⁷ Comparisons of blood lead and tibia lead may indicate whether the effect of lead on blood pressure is an acute effect of recent dose or a chronic effect of cumulative dose. In a prior study of an older cohort with previous high occupational exposure to organic and inorganic lead, we found that both blood lead at baseline and tibia lead at the third clinic visit were associated with annual change in systolic blood pressure.¹ Because the associations were of similar strength, and all subjects were former workers without recent occupational exposure to lead, we were not able to disentangle the relative importance of the 2 lead biomarkers. Lead content in bone tissue contributes to the concentration of lead in blood through the process of bone remodeling.^{8,9} Because this population was older and had no current lead exposure, their blood lead concentrations were probably significantly influenced by their bone lead content.

In this study, we report on an occupational cohort used in lead-using facilities in South Korea. In contrast to subjects

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in our previous study, participants were younger and most had substantial current exposure to lead. For each subject, we obtained multiple measures of blood lead, tibia lead, and blood pressure over 3 years. The study design allowed us to compare associations with blood lead and tibia lead, and to make inferences about the acute and chronic effects of recent and cumulative lead dose.

METHODS

Study Population, Study Design, and Follow-Up

We followed an occupational cohort employed at 26 lead-using facilities in South Korea between October 1997 and June 2001. A detailed description of the study population and study design has been reported previously.^{10–13} The study was reviewed and approved by the Institutional Review Boards at the Johns Hopkins Bloomberg School of Public Health (Baltimore, Maryland) and the Soonchunhyang University School of Medicine (Chonan, South Korea). All participants provided written informed consent. Participation generally exceeded 80% in the lead-using facilities, but was lower in 4 of the 26 facilities (less than 60%). Of 805 enrolled lead workers, complete follow-up (3 visits) was attained for 575 subjects (71%) with blood pressure measurements, whereas 127 (16%) participated in the baseline visit and either the second or third visit. One hundred three subjects (13%) completed only the baseline visit. This report describes analyses for the 575 workers with complete data for 3 visits. Of these, 504 workers had current inorganic lead exposure and 71 workers no longer had positions with lead exposure. During the study, 78 additional workers left their lead-exposed jobs. All “retired” workers were retained in the cohort and were included in our analyses. The mean \pm standard deviation (SD) number of years elapsed between visits 1 and 2 was 1.03 ± 0.21 (range = 0.60–2.30) and between visits 1 and 3 was 2.12 ± 0.43 (range, 1.58–3.58).

Data Collection

At the first visit, subjects completed a standardized questionnaire concerning personal characteristics and behaviors, a medical history, and an occupational history.¹¹ These data were updated at subsequent visits along with repeated measurements of blood pressure, height, and weight. Biologic samples included a blood specimen (each visit), a spot urine sample (each visit), and tibia lead concentration (visits 1 and 2). Blood specimens (10 mL) were collected by venipuncture and stored at -70°C as whole blood, plasma, and red blood cells. Blood lead was measured with a Zeeman background-corrected atomic absorption spectrophotometer (model 8100; Hitachi Ltd. Instruments, Tokyo, Japan) at the Institute of Industrial Medicine, a certified reference laboratory for lead in Korea.¹⁴ Tibia lead was measured using x-ray fluorescence in units of micrograms of lead per gram of bone mineral ($\mu\text{g/g}$). Blood pressure (systolic and fifth Korotkoff diastolic) was measured at each visit using a Hawksley random zero sphygmomanometer (Hawksley, Sussex, U.K.) according to the Johns Hopkins Welch Center for Prevention, Epidemiology, and Clinical Trials protocol.¹² Three measurements,

using an appropriately sized cuff, were taken by a physician trained in the method 5 minutes apart with the subject sitting.

Statistical Analysis

Conceptual Basis

Our primary interest was to determine whether the effect of lead on blood pressure was due to acute effects from recent exposure or due to chronic effects (that can be persistent) from cumulative lead exposure. Accordingly, we used methodology modeling blood pressure in terms of different aspects of the history of lead dose acquisition for an individual. This methodology for the analysis of data from prospective observational studies with repeated measurements of dependent and independent variables has been described by several statistical authors^{15–17} as well as in a previous paper on neurobehavioral outcomes in this cohort.¹⁰ The model accommodates the simultaneous evaluation of multiple lead dose measures for an individual that include recent and cumulative dose measures. It also differentiates cross-sectional versus longitudinal relationships between dose and health. We were interested in whether longitudinal relationships differed from their cross-sectional counterparts, which would indicate cohort, selection, or other biases in the cross-sectional associations.

We had measures of blood lead for each visit in this cohort. We constructed a measure ($PbB_{i,t}$) of blood lead at the baseline visit (V1) as well as a variable for the longitudinal change in blood lead concentration from the baseline to the second visit and from the second visit to the last visit ($PbB_{i,t} - PbB_{i,t-1}$; $t = 2, 3$). Lead in blood has an average half-life of 30 days. Thus, these dose measures can be interpreted to reflect recent dose or change in recent dose, respectively.

We also wanted to evaluate a possible chronic effect of accumulated lead body burden. We used tibia lead concentration measured at time, $t-1$ ($TIB_{i,t-1}$), to estimate a historical measure of cumulative lead dose (in other words, to evaluate whether tibia lead at visit 1 or visit 2 predicted change in blood pressure over the next year). The average half-life of lead in tibia bone is on the order of decades, and tibia lead concentration does not change appreciably over the short-term. Therefore, associations with tibia lead can be interpreted as the effect of lifetime lead accumulation.

Certain variables that could be constructed were not investigated. Historical associations with blood lead were not examined because a blood lead level predicting change in health over the next year was not deemed to be biologically sensible. A longitudinal measure for tibia lead was not evaluated because annual change in tibia lead levels could not be validly measured with the equipment that was then in use; the error in tibia lead measurement was larger than the change in tibia lead levels during the course of 1 year.

We examined the cross-sectional, historical, and longitudinal blood or tibia lead measures in 4 models of blood pressure change to distinguish various effects of lead (Table 1): short-term change associated with recent dose (model 1); longer-term changes associated with cumulative dose, controlling for the baseline association of recent (model 2) or

TABLE 1. Patterns of Associations Using Longitudinal Models

Model	Cross-Sectional (β_C)		Historical (β_H)	Longitudinal (β_L)	Inference
	Blood Lead	Tibia Lead	Tibia Lead	Blood Lead	
1	+			+	Short-term, probably reversible, change associated with recent dose
2	+		+		Longer-term, possibly irreversible or progressive, change associated with cumulative dose (controlling for cross-sectional influence of recent dose)
3		+	+		Longer-term, possibly irreversible or progressive, change associated with cumulative dose (controlling for cross-sectional influence of cumulative dose)
4	+		+	+	Both short-term change with recent dose and longer-term change with cumulative dose

cumulative (model 3) dose with baseline blood pressure; or a combination of these effects (model 4). These models were formulated before examination of the data in accordance with our understanding about the kinetics and toxicity of lead to facilitate biologic interpretations and minimize chance associations.

The following equations were used to evaluate model 4 (Table 1) using systolic blood pressure (SBP) as the dependent variable, cross-sectional and longitudinal terms for blood lead, and an historical term for tibia lead. A complete description of the regression equations corresponding to each of the models found in Table 1 is provided in the Appendix available with the online version of this article.

For visit 1

$$SBP_{i,1} = \beta_{01} + \beta_C (PbB_{i,1}) + \varepsilon_{i,1} \quad (1)$$

where $i = i^{th}$ individual and $1 =$ visit 1; $\varepsilon_{i,1}$ is residual error; and C designates “cross-sectional.” Thus, β_C summarizes the baseline cross-sectional relationship between SBP and blood lead.

For visit 2

$$SBP_{i,2} = \beta_{02} + \beta_C (PbB_{i,1}) + \beta_H (TIB_{i,1}) + \beta_L (PbB_{i,2} - PbB_{i,1}) + \varepsilon_{i,2} \quad (2)$$

where H designates “historical” and L designates “longitudinal.”

For visit 3

$$SBP_{i,3} = \beta_{03} + \beta_C (PbB_{i,1}) + \beta_H (TIB_{i,1} + TIB_{i,2}) + \beta_L (PbB_{i,3} - PbB_{i,1}) + \varepsilon_{i,3} \quad (3)$$

Equations 1 to 3 can be combined to derive equations for change from visit 1 to visit 2 (equation 4), and change from visit 2 to visit 3 (equation 5), as follows.

For average change from visit 1 to visit 2 (subtracting equation 1 from equation 2 [intercepts not shown]).

$$Av (SBP_{i,2} - SBP_{i,1}) = \beta_H (TIB_{i,1}) + \beta_L (PbB_{i,2} - PbB_{i,1}) \quad (4)$$

For average change from visit 2 to visit 3 (subtracting equation 2 from equation 3).

$$Av (SBP_{i,3} - SBP_{i,2}) = \beta_H (TIB_{i,2}) + \beta_L (PbB_{i,3} - PbB_{i,2}) \quad (5)$$

Thus, from equations 4 and 5, the historical β coefficients (β_H) summarize prediction of change in systolic blood pressure from time t to time $t + 1$ (visit 1 to visit 2 or visit 2 to visit 3, respectively) by tibia lead at time t (visit 1 or visit 2). The longitudinal β coefficients (β_L) summarize prediction of change in systolic blood pressure from time t to $t + 1$ by change in blood lead from time t to time $t + 1$. If $\beta_L = \beta_C$, then models for visits 2 and 3 reduce to a “simplified” model $SBP_{i,t} = \beta_o + \beta_C (PbB_{i,t}) + \beta_H [TIB_{i,1} + (t-2)TIB_{i,2}] + \varepsilon_{i,t}$. Subtracting the equations for 2 visits then summarizes the association of change in blood pressure with change in blood lead. Fitting the simplified model both validly estimates the shared effect $\beta_C = \beta_L$ and gains precision for such estimations over the more complex approach.

Modeling

Summary statistics were calculated for each lead dose variable, blood pressure, and subject-specific characteristics. Graphic representations of blood pressure and lead concentrations were examined in relation to each other and over time. The longitudinal data were analyzed in multivariate models using generalized estimating equations (GEE) and the STATA Statistical Software Release 7.0 (Stata Corp., College Station, TX). Values for the cross-sectional, historical, and longitudinal lead variables were assigned for each subject for each visit as indicated in equations 1 through 3.

The GEE model allows for control of the correlation between repeated measures for an individual. We used an unstructured correlation structure (ie, we did not constrain the correlations to be the same across all of each worker’s visits).

The variance of the model coefficients was estimated using the Huber-White sandwich estimator of variance. In addition to the lead dose variables, final models included variables for visit number, age at baseline, baseline age squared, baseline lifetime alcohol consumption (4 categories), baseline body mass index (kg/m^2), sex, and baseline use of blood pressure-lowering medications. Inclusion of indicator terms for cigarette smoking (never, current, exsmoker), education (no high school, high school attendance but not graduation, high school graduate, postsecondary education), and a continuous variable for job duration did not predict systolic blood pressure and did not alter the value of the regression coefficients for lead dose. These variables were not included in the final models. Mean lead biomarker concentrations and distributions for age, smoking status, and drinking habit varied between the male and female workers (Table 2). Therefore, we checked the results of the final model using the combined cohort by reanalyzing the model separately for men. Final models were checked for linearity, influential points, and homoscedasticity by examining residuals and partial residual plots.

TABLE 2. Baseline Characteristics of Subjects With Complete Visit Data, Korea Lead Study, 1997–2001

Characteristic	Women (n = 140)	Men (n = 435)
Age (years); %		
18–29	1	18
30–39	9	38
40–49	39	33
50–65	51	12
Education; %		
No high school	72	14
No high school graduation	17	27
High school graduation	10	51
Postsecondary education	1	9
Hypertension (yes/no)*; %	2	8
Blood pressure (mm Hg); mean \pm SD		
Systolic		
Visit 1	124.6 \pm 20.5	122.8 \pm 15.0
Visit 2	123.9 \pm 19.7	121.1 \pm 15.0
Visit 3	124.2 \pm 21.5	120.0 \pm 14.3
Diastolic		
Visit 1	76.4 \pm 12.6	75.9 \pm 11.6
Visit 2	75.8 \pm 12.0	74.1 \pm 12.8
Visit 3	74.8 \pm 13.2	74.0 \pm 12.4
BMI (kg/m^2); mean \pm SD	24.7 \pm 3.5	22.6 \pm 2.7
Smoking status; %		
Nonsmoker	98	16
Current	1	69
Exsmoker	1	15
Alcohol status; %		
Nondrinker	73	18
Current	24	76
Exdrinker	3	6
Job duration (years); mean \pm SD	7.5 \pm 4.8	8.8 \pm 6.7

*Physician's diagnosis or current medication use reported at any visit.

Intercepts for each company were added to the final models to explore potential confounding of the lead exposure – blood pressure relation by employment location. The models also were evaluated after excluding subjects defined to be hypertensive. Subjects were defined to have hypertension if they reported taking medications to control blood pressure or they had received a physician's diagnosis of hypertension.

RESULTS

Demographics and Lead Dose Measures

At baseline, the mean \pm SD age of the cohort was 41.4 \pm 9.5 years (range = 18.2–64.8), and they had worked an average of 8.5 years (range = 0–36.2) in lead-exposed jobs. Female workers made up 24% of the cohort with complete follow-up (Table 2). Compared with the male lead workers, the women were older, less well educated, and primarily nonsmokers (97%) and nondrinkers (73%). Although female workers had been employed in lead-exposed jobs for a comparable period of time, blood lead and tibia lead concentrations were approximately 40% lower than those of the male lead-exposed workers. Systolic and diastolic blood pressure and body mass index were similar in men and women.

On average, blood lead concentrations remained constant among male and female lead workers over the 3-year follow-up period (Table 3). Tibia lead concentrations declined from visit 1 to visit 2 on average, a decline that was attributable primarily to workers at 5 plants where baseline tibia lead was determined at the plant instead of the university clinic. This reduction was not expected. Because this may reflect interference with tibia lead measurements by ambient lead levels on-site, a sensitivity analysis was conducted excluding individuals from the 5 plants where baseline tibia measurements were taken on-site.

Systolic and Diastolic Blood Pressure Change Over Time

Average systolic blood pressure decreased slightly from 123 to 120 mm Hg among men during the study but remained constant among women. Average diastolic blood

TABLE 3. Lead Concentrations in Blood and Bone of Subjects With Complete Visit Data

Lead Concentration	Women (n = 140) Mean \pm SD	Men (n = 435) Mean \pm SD
Blood lead ($\mu\text{g}/\text{dL}$)		
Visit 1	20.3 \pm 9.6	35.0 \pm 13.5
Visit 2	20.8 \pm 10.8	36.5 \pm 14.2
Visit 3	19.8 \pm 10.7	35.4 \pm 15.9
Tibia lead ($\mu\text{g}/\text{g}$)		
Visit 1	28.2 \pm 19.7	41.7 \pm 47.6
Visit 2	22.8 \pm 20.9	37.1 \pm 48.1
Patella lead ($\mu\text{g}/\text{g}$)		
Visit 3	49.5 \pm 38.5	87.7 \pm 117.0

pressure also decreased from 76 to 74 mm Hg among males and remained constant among females.

Association With Blood Lead

The average change in systolic blood pressure between visits was associated with the change in blood lead concentration between visits in models with and without tibia lead terms (Table 4: models 1, 2, and 4). Systolic blood pressure at baseline was associated with baseline blood lead concentration. Both blood lead variables (cross-sectional and longitudinal blood lead) predicted approximately the same increase in systolic blood pressure: 1 mm Hg per 10- μ g/dL increase in blood lead. The predicted change was not altered when subjects with hypertension were excluded from the model (Table 4) or when indicator variables for each plant were included in the statistical model (not shown).

In the simplified GEE model containing blood lead ($PbB_{i,t}$) plus the historical tibia lead term and other covariates, blood lead levels were associated with an increase of 0.09 mm Hg/ μ g/dL (95% confidence interval = 0.03 to 0.15). Average annual change in diastolic blood pressure was not associated with blood lead levels.

Association With Tibia Lead

Systolic blood pressure at the baseline examination was not associated with tibia lead concentration at baseline (Table 4: models 2, 3, and 4). We found that historical tibia lead was inversely associated with change in systolic blood pressure, although the magnitude of the association was small. The results were not changed when we reexamined the models excluding workers from the 5 plants where contamination was suspected. Average annual change in diastolic blood pressure was not predicted by tibia lead dose (data not shown).

DISCUSSION

We tested 4 models of blood pressure change that described different aspects of its possible relation with lead dose. We found that annual change in blood lead concentration was associated with the annual change in systolic blood pressure when traditional risk factors for high blood pressure were controlled. These data suggest that systolic blood pressure may respond in a relatively short timeframe to recent

lead exposure. The regression coefficient for the annual change in blood lead indicates that systolic blood pressure increases by almost 1 mm Hg with each 10- μ g increase in blood lead per year. This is a relatively small annual effect for an individual but suggests that reduction of lead exposure could have an important impact on the health of a population over time.

An alternative explanation is that factors that alter blood lead change in individuals, if associated with change in blood pressure, may be responsible for the observed association. Blood lead and tibia lead concentrations are subject to measurement error, including regression to the mean, within-person variability, and technical error. Blood lead is associated with less measurement error than tibia lead in cross-sectional analysis, but the relative size of the error associated with the change in blood or tibia lead may be different. Another factor is changing work conditions or job status (eg, retirement or switching between jobs with different lead exposure) that results in real changes in lead dose. A strength of this study is that although some workers in this cohort "retired" from lead-exposed jobs, they were retained in the cohort and were included in the analysis. Finally, individual differences in the toxicokinetics of lead would lead to variation in blood or bone concentration for a given exposure level and duration. We do not think that any of these reasons for change in lead dose would be related to blood pressure status, however.

The ability to analyze change in blood pressure in relation to change in blood lead using repeated measures was a strength of the study. This study design mitigated some problems encountered in cross-sectional analyses, including selection and cohort bias, which can result in biased effect estimates. The longitudinal terms in our models summarize change-on-change relationships, which advantageously treat individuals as their own controls. Moreover, our estimates of the longitudinal relationship of systolic blood pressure with changes in recent dose were similar to estimated cross-sectional terms characterizing the baseline association between recent dose and systolic blood pressure. This consistency suggests that the observed cross-sectional relationship with recent dose was not appreciably biased in our study.

Modeling effects of time-varying covariates is complicated by the potential for endogeneity, whereby past out-

TABLE 4. Four Models of the Association of Blood and Tibia Lead With Systolic Blood Pressure

Model*	Blood Lead β_C (95% CI)	Tibia Lead β_C (95% CI)	Tibia Lead β_H (95% CI)	Blood Lead β_L (95% CI)
1	0.08 (-0.01 to 0.16)			0.09 (0.01 to 0.16)
2	0.09 (-0.002 to 0.18)		-0.02 (-0.03 to -0.01)	
3		0.01 (-0.02 to 0.04)	-0.02 (-0.03 to 0.004)	
4	0.10 (0.01 to 0.19)		-0.02 (-0.03 to -0.01)	0.09 (0.02 to 0.16)
4 excluding hypertension [†]	0.09 (0.002 to 0.18)		-0.02 (-0.03 to -0.002)	0.08 (0.01 to 0.16)

*Final models included covariates for visit, baseline age, baseline age squared, categories of lifetime alcohol consumption, body mass index, gender, and use of blood pressure-lowering medications.

[†]Hypertension was defined as a report of a physician's diagnosis of hypertension or taking medications to control high blood pressure.

CI indicates confidence interval.

comes may predict future covariates independently of past covariate values. Research over the past decade has elucidated that this endogeneity poses particular challenges for GEE with unstructured covariance matrices such as we have used.^{18,19} It seems conceptually unlikely that past blood pressure values should predict subsequent changes in blood lead independent of past blood lead values; however, the fact of measurement error in blood lead levels implies we cannot rule out such a phenomenon. We therefore reran our models with an independence working covariance matrix (with robust variance estimation to ensure validity of standard errors). Material findings did not change; however, we did observe an increase in the magnitude of the longitudinal blood lead coefficient. Thus, if anything, our primary findings with respect to blood lead may be conservative.

The addition of historical tibia lead to the model (models 2 and 4) did not reduce the magnitude of the risk predicted by cross-sectional or longitudinal blood lead. Rather, confidence intervals around the regression coefficient for blood lead narrowed when tibia lead terms were included in the model (model 4). To further understand the complex relations between blood lead and tibia lead over time, we examined graphic displays of blood lead change from one visit to the next by the tibia lead at the prior clinic visit (eg, blood lead change between visit 1 and visit 2 by tibia lead at baseline, and blood lead change between visit 2 and visit 3 by tibia lead at visit 2) (data not shown). The plots showed that the variability of the change in blood lead between visits at each level of tibia lead decreased as tibia lead concentration increased, probably due to physiological dampening.²⁰ If tibia lead only affects blood pressure through its influence on blood lead concentration, then the strength of the association of blood lead change on blood pressure change may depend on the level of lead in bone stores.

It should be noted that blood lead at baseline also was associated with blood pressure at baseline, so the total effect of lead on blood pressure was not limited to the longitudinal relation alone. This association was demonstrated in a relatively young, working population with a low prevalence of existing hypertension. Although the study population contained individuals with high lead exposure and the range of blood and tibia lead concentrations was wide, 5% of the cohort with full data had blood concentrations ≤ 10 $\mu\text{g}/\text{dL}$ and tibia lead concentrations ≤ 5 $\mu\text{g}/\text{g}$. Cumulative lead burden may exert more influence on blood lead levels and consequently on blood pressure in an aging population with more prolonged lead exposure such as the U.S. population we studied previously.¹

The lack of biologic independence between blood and bone lead compartments is important to consider when interpreting the statistical models. The models assume that recent and cumulative lead exposure is represented separately by blood lead and tibia lead, respectively. However, a cross-sectional blood lead association with blood pressure at baseline may reflect recent as well as cumulative lead dose effects.

The direction of the effect estimates for historical tibia lead is difficult to explain physiologically, although the size of predicted systolic blood pressure change with unit change in historical tibia lead is exceedingly small. Furthermore,

some of the association of historical tibia lead with change in blood pressure could be captured by the cross-sectional blood lead term if baseline blood lead is correlated with tibia lead and blood pressure at baseline is correlated with change in blood pressure over time.

Tibia lead at baseline was not associated with baseline systolic blood pressure in this cohort among subjects with data for 3 visits or among all subjects.¹² Another longitudinal analysis of blood pressure effects, with comparisons of blood and bone lead measures, reported an association between patella lead at baseline and the incidence of hypertension between 1991 and 1997 among participants in the Normative Aging Study in the eastern United States.⁵ Patella contains trabecular bone, a compartment with a higher rate of exchange with blood.⁹ The association with tibia lead was not as strong, and no association was found for baseline blood lead. The different lead dose associations between that study and our study may be explained by differences in population genetics or demographics or the analytic methods used. The South Korean occupational cohort was younger than subjects in the Normative Aging Cohort in the United States and had concurrent lead exposure. Other studies evaluating cross-sectional associations have reported a stronger relation of blood lead with blood pressure or hypertension among younger individuals.^{21,22} In addition, we evaluated blood pressure change in the Korean cohort, whereas the U.S. study considered hypertension incidence. We did not have the power to evaluate hypertension incidence in this population.

This study in occupationally exposed subjects in South Korea indicates that lead exposure may act continuously on systolic blood pressure and reductions in exposure may contribute to reductions in blood pressure. On the other hand, cumulative lead burden may contribute to hypertension incidence by other mechanisms, especially over longer periods of time and in older subjects. The present analysis in relatively young subjects with a low prevalence of hypertension suggests that at least one of the biologic pathways that influences how systolic blood pressure responds to lead operates over a relatively rapid timeframe.

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