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Mortality among participants in a lead surveillance program

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ABSTRACT

Background: There is evidence that adult lead exposure increases cancer risk. IARC has classified lead as a 'probable' carcinogen, primarily based on stomach and lung cancer associations.
Methods: We studied mortality among men in a lead surveillance program in 11 states,. categorized by their highest blood lead (BL) test (0– < 5 μg/dl, 5– < 25 μg/dl, 25– < 40 μg/dl and 40+ μg/dl).
Results: There were 58,368 men with a median 12 years of follow-up (6 to 17 years from lowest to higher BL category), and 3337 deaths. Half of the men had only one BL test. There was a strong healthy worker effect (all cause SMR=0.69, 95% CI: 0.66–0.71). The highest BL category had elevated lung and larynx cancer SMRs (1.20, 95% CI: 1.03–1.39, n=174, and 2.11, 95% CI: 1.05–3.77, n=11, respectively); there were no significant excesses of any other cause-specific SMR. Lung cancer RRs by increasing BL category were 1.0, 1.34, 1.88, and 2.79 (test for trend $p= < 0.0001$), unchanged by adjustment for follow-up time. The lung cancer SMR in the highest BL category with 20+ years follow-up was 1.35 (95% CI: 0.92–1.90).
Conclusions: We found an association of blood lead level with lung cancer mortality. Our data are limited by lack of work history (precluding analyses by duration of exposure), and smoking data, although the strong positive trend in RRs by increasing blood lead category in internal analysis is unlikely to be caused by smoking differences. Other limitations include different lengths of follow-up in different lead categories, reliance on few blood lead tests to characterize exposure, and few deaths for some causes.

1. Introduction

With the reduction of lead use in commercially available products (particularly leaded gasoline), ambient lead exposure has been reduced since the 1970s. However, occupational exposure continues to be important. The National Institute of Occupational Safety and Health (NIOSH) estimated in the 1980s that more than 3 million workers in the US were potentially exposed to lead (Staudinger and Roth 1998). More recent estimates can be made using data from NIOSH's Adult Blood Lead Surveillance (ABLES) program; data from 37 states indicated that approximately 130,000 workers had been tested for blood lead in 2005 (www.cdc.gov/niosh/topics/ABLES/pdfs/2002-2005lead_data.pdf).

The current US OSHA standard calls for workers to be removed from exposure when they have a blood lead of 50 μg/dl (construction workers), or 60 μg/dl (other workers), and to not return until their blood lead drops below 40 μg/dl (www.osha.gov/SLTC/lead/). A number of authors have called for removal of workers from exposure when blood levels reach 20 μg/dl (Hu et al. 2007, Kosnett et al., 2007, Schwartz and Hu, 2007, Spivey 2007).

Adult chronic exposure to lead has been associated with multiple outcomes, although evidence is not conclusive. Both the International Agency for Research on Cancer (IARC) and the National Toxicology Program have concluded that lead is a probable human carcinogen, based primarily on evidence of the impacts of lead exposure on lung and stomach cancers and some suggestion of an effect on kidney and brain cancer (IARC, 2006, NTP, 2004). Lead exposure has been associated with modest increases in blood pressure. A meta-analysis of 31 studies by Nawrot et al. (2002) found that most showed a positive association between blood lead and blood pressure after controlling for age; a doubling of blood lead was associated with a 1.0 mm rise in systolic pressure (95% CI 0.5–1.4), and a 0.6 mm Hg increase in diastolic pressure (95% CI 0.4–0.8). Increased blood pressure is a risk factor for stroke and heart disease, but information on these outcomes is limited in the current literature. In a review of articles concerning lead and the risk of cardiovascular disease (CVD), Navas-Acien et al.(2007) found that overall there was insufficient epidemiological data to draw conclusions.

Abbreviations: ABLES, Adult blood lead epidemiology and surveillance; NIOSH, National Institute for Occupational Safety and Health; BL, Blood lead; μg/dl, microgram/deciliter; HWE, healthy worker effect; SMR, standardized mortality ratio; RR, rate ratio

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Very high levels of lead in the body are known to result in kidney failure (US EPA 2005), but effects at low levels are less clear. A recent comprehensive review of lead-related nephrotoxicity concluded that lead contributes to nephrotoxicity, even at blood lead levels below 5 μg/dl, especially in people with other illnesses such as hypertension and diabetes (Ekong et al. 2006).

The objective of the current study was to evaluate the association of lead exposure and subsequent all-cause and cause-specific mortality, using data from 11 states participating in NIOSH's ABLES program.

2. Methods

2.1. Data sources/study participants

The Adult Blood Lead Surveillance program, sponsored by NIOSH, started collecting state-level data on blood lead levels in 1987 (Roscoe et al. 2002). Initially, some states gathered data only on individuals whose blood lead levels exceeded 25 μg/dl, but subsequently many states began to collect data on subjects with lower blood lead levels. Blood lead tests were conducted primarily in response to occupational exposure, but in some cases stemmed from non-occupational exposure. ABLES coverage increased from 4 states in 1987 to 41 states in 2012 (www.cdc.gov/niosh/topics/ABLES/description.html).

NIOSH has collected data on industry of employment for a limited number of ABLES subjects ($n=6999$) with blood lead levels $\geq$ 25 μg/dl (CDC, 2011). Of these 62% were in manufacturing, 10% in construction, 7% in metal mining, 1% in trade (scrap and waste materials), and 20% were in other industries or data were unavailable.

We obtained data from 11 state ABLES programs: Connecticut, California, Ohio, Minnesota, Iowa, Pennsylvania, New York, New Jersey, Wisconsin, Michigan and Massachusetts, from their year of first participation until 2005. The percentage of the cohort represented by these states was 4%, 18%, 10%, 2%, 3%, 3%, 29%, 11%, 6%, 3%, and 11% respectively. These states were chosen because they had the most subjects with blood lead data, and data which went back the farthest in time. We excluded any subjects missing information on date of birth, test date, or blood lead levels. We categorized each blood lead level reading into 1 of 4 categories, namely <5 μg/dl, 5 to <25 μg/dl, 25 to <40 μg/dl, and 40+ μg/dl. The categories <25, 25–40, and 40+ μg/dl have been traditionally used to categorize occupational blood lead levels; the lowest category of 5 μg/dl was considered equivalent to non-occupational US blood lead levels.

The data uniformly available from the states consisted of name, date of birth, gender, data of each blood test, and blood lead level for each test. Additional incomplete data was available on race (69% missing) and social security number (SSN; 74% missing). We classified those with missing race as white in our primary analyses, since 86% of subjects among those with known race were white. We also conducted sensitivity analyses using imputed race, but resulted in virtually identical results, and are not presented here. There were no data on work history or smoking. Data on type of occupation or industry were collected sporadically in only some states for limited numbers of subjects.

Data from ABLES were matched to the National Death Index (NDI) to assess mortality outcomes among the cohort. For efficiency and cost considerations, we selected a subset of the full cohort for the NDI matching process, while maintaining sufficient power to analyze the association of blood lead categories and mortality. We first selected all subjects from the states who had ever had a blood lead level in categories 3 or 4. We then randomly selected an equal number of people from categories 1 and 2 (50% from each category), stratified by state. Finally, we restricted our cohort to males, because females represented only 15% of the population, were younger than the men (few deaths), were highly concentrated in the lowest blood lead category, and were more likely to have been tested for non-occupational reasons, such as during pregnancy (personal communication, Susan Payne, California ABLES/Occupational Lead Poisoning Prevention Program (OLPPP), May 2013). We further excluded all people who were tested for the first time after the age of 70 years or before the age of 18 years, and any blood tests we considered implausible (greater than 250 μg/dl, as these values were considered implausible).

After the above exclusions and accounting for subjects with test results in multiple states (for whom data had to be merged under a single identification number), we had a final analytic dataset with 58,368 unique subjects. About half the subjects (49%) had a single blood test, while the remainder had a median of four. Considering each blood lead test an observation, we had a total of 283,270 observations. For epidemiologic analyses, blood lead category for each individual was defined as the highest category ever achieved; hence peak exposure was our variable of interest for those who had more than one blood test. It should be noted that blood levels for the majority of subjects with multiple tests were generally in the same blood lead category (see Results).

We used name, date of birth, gender, race (when available) and SSN (when available) for matching with the NDI database through the end of 2010, to obtain data on date and cause of death (underlying and multiple). Three states sent in their own data to NDI; their follow-up ended in 2009 (Massachusetts) or 2008 (Wisconsin, Michigan). To determine if a match with the NDI was a true match from amongst the multiple matches reported by NDI, we only selected those who were assigned a status code of 1 by NDI, indicating a high probability of a match. If a person's last blood lead test date was after their date of death, then the match was dropped and these subjects were considered as alive. If there were multiple matches with status code 1, we selected the one with the highest NDI probability score for a match.

2.2. Analyses

The NIOSH Life Table Analysis System (NIOSH, LTAS, Version 3.3) was used to calculate cause-specific rates of death for the cohort, and to compare these rates with those of the US population via standardized mortality ratios (SMRs), adjusted for age (five-year categories), race, sex, and five-year calendar time period (person-time at risk and observed events were categorized into strata defined by these variables) (Schubauer-Berigan et al. 2011). Overall, we had information on 92 causes of death; we present SMRs for 11 specific causes of death of *a priori* interest for lead exposure, including cancers (lung, brain, kidney, stomach, esophagus, larynx, bladder, stroke, chronic obstructive pulmonary disease (COPD), ischemic heart disease, and chronic renal disease. In the SMR calculation, US national mortality rates were used rather than those from the 11 different states, for convenience and because mortality rates in the 11 states (which represent about a third of the US population) as a whole reflect national rates. A weighted average of

Table 1
Demographics of the Cohort.

Characteristics	Highest lead category achieved				Total
	1 0– <5 μg/dl	2 5– <25 μg/dl	3 25– <40 μg/dl	4 40+ μg/dl	
Total	6848 (11.7%)	18,650 (31.9%)	21,448 (36.7%)	11,422 (19.6%)	58,368
Median years of follow-up	6.4	9.9	14.2	17.1	12
Mean age at first test	40.7	39.9	37.9	38.3	38.9
Race					
White	1,448 (21%)	2356 (13%)	6246 (29%)	4339 (38%)	14,389 (26%)
Non-white	252 (4%)	558 (3%)	1673 (8%)	1200 (10%)	3683 (6%)
Missing/unknown	5148 (75%)	15,736 (84%)	13,529 (63%)	5883 (52%)	40,296 (69%)
% Non-white among known race	0.13	0.14	0.12	0.12	0.14
Median number of observations in those with > 1	2	3	4	6	4
% With single observations	6124 (89%)	12,739 (68.3%)	7786 (36.3%)	1940 (16.9%)	28,589 (48.9%)
Mean highest blood lead level	3	13	31)	52	26
% With SSN (for matching)-Overall[a]	611 (9%)	2084 (11%)	7664 (36%)	4883 (43%)	15,242 (26%)
Median year of birth	1962	1961	1959	1955	1959
Median year of death	2006	2005	2004	2003	2004
Number dead	173 (2.5%)	635 (3.4%)	1301 (6.1%)	1228 (10.8%)	3337 (5.7%)

[a] Three states, WI, MI, MA sent their own data and sent us de-identified data, without SSN; hence these percentages are underestimates.