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Childhood lead exposure and uptake in teeth in the Cleveland area during the era of leaded gasoline

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ABSTRACT

Childhood uptake of lead from exposure to atmospheric leaded gasoline in the United States has been studied using mainly blood lead levels. Since reliable blood lead techniques were used only after the peak use of leaded gasoline, the prior exposure history is unclear. The well-documented decline in blood lead levels after the mid-1970s could represent the continuation of a historic steady decline in exposure from many sources. Alternatively, the post-1970s decline might represent the declining phase of a unimodal rise and fall corresponding closely to usage of leaded gasoline. To assess these possibilities, lead concentration and 207Pb/206Pb isotope ratios were measured in the enamel of permanent molar teeth formed between 1936 and 1993 in mainly African-American donors who grew up in the Cleveland area. Tooth enamel preserves the lead concentration and isotope ratio that prevails during tooth formation. Historical trends in enamel lead concentration were significantly correlated with surrogates of atmospheric lead exposure: lead in sediments of two dated Lake Erie cores, and lead consumed in gasoline. About two-thirds of the total lead uptake into enamel in this period was attributable to leaded gasoline, and the remainder to other sources (e.g. paint). Enamel 207Pb/206Pb isotope ratios were similar to those of one lake sediment. Multivariate analysis revealed significant correlation in neighborhoods with higher levels of traffic, and including lake sediment data, accounted for 53% of the variation in enamel lead levels. Enamel lead concentration was highly correlated with reported African-American childhood blood levels. The extrapolated peak level of 48 μg/dL (range 40 to 63) is associated with clinical and behavioral impairments, which may have implications for adults who were children during the peak gasoline lead exposure. In sum, leaded gasoline emission was the predominant source of lead exposure of African-American Cleveland children during the latter two-thirds of the 20th century.

1. Introduction

Beginning in the 1970s, the blood lead levels (PbB) of American children declined along with the usage of leaded gasoline and atmospheric lead concentration (Billick et al., 1979; Annest et al., 1983; Rabinowitz et al., 1984; US EPA, 1986; Schwartz and Pitcher, 1989; review, Thomas et al., 1999). Analogous data were obtained from a comparison of deciduous tooth lead in the 1970s vs. the 1990s (Tvinnereim et al., 1997). However, the level of lead uptake in earlier years, during the introduction of leaded gasoline, is unknown because analyses of PbB prior to the peak of leaded gasoline usage were considered unreliable because of contamination (Patterson and Settle, 1976; Everson and Patterson, 1980; Thomas, 1995). Given the known exposure of children, prior to the 1970s, to other major lead sources, such as leaded paint (Weaver, 1989, Nriagu, 1990; President's Task Force, 2000; Jacobs et al., 2002) and soldered food cans (Jelinek, 1982; Bolger et al., 1992; National Research Council, 1993), at least two scenarios could describe the lead burden of American children through the period when leaded gasoline was introduced and later phased out (from about 1930 to 1990).

In the first scenario, exposures to other major pre-existing lead sources (paint, solder in food cans) would themselves have produced high PbB levels prior to the 1930s so that the additional exposure to newly introduced leaded gasoline might have modestly increased PbB. Indeed, Facchetti (1989) reported that airborne lead contributed only 24% to PbB (bone and non-atmospheric sources contributing the remainder). Leaded paint was used in most housing until the 1940s

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(Weaver, 1989) and in a substantial number of houses until about 1960 (President's Task Force, 2000; Jacobs et al., 2002). Indeed, in much of the Cleveland population of this study, such housing was not substantially replaced over the next 30 years. Solder in food cans, said to account for 20–30% of dietary lead intake (US EPA, 1977; US EPA, 1986), could also have been a major source of lead uptake. For instance, in New Zealand, PbB fell nearly two-fold from 1978 to 1985, presumably due to decreased use of leaded food cans, because lead in gasoline and in drinking water was constant (Hinton et al., 1986). In the US, canned infant milk had high levels of lead until the 1970s (Jelinek, 1982) and 90% of food cans were lead-soldered as late as 1979, declining to 6% by 1988 (Bolger et al., 1992). As explained in Methods, drinking water and atmospheric industrial sources were probably not major lead sources in the Cleveland area. Thus, if lead in paint or food was already causing substantially high PbB before the advent of leaded gas, population lead levels would already have been high before the advent of leaded gasoline. Therefore, the decline of PbB after the 1970s could have resulted from the combined phase-out of leaded gasoline, lead in food cans, and lead in paint.

In the second scenario, pre-existing lead exposure sources would have been small compared to lead exposure due to newly introduced gasoline, so that PbB plotted over time would be predicted to be a unimodal curve, increasing to a maximum and then decreasing, and closely corresponding to the rise and fall of leaded gasoline and atmospheric lead.

The choice between these two scenarios is of public health significance because the severity of clinical and behavioral effects of lead increases with uptake (ATSDR, 2007). Thus, the first and second scenarios would predict different expected impacts of lead exposure on populations now living who were children from about 1930 to 1985), depending on whether (scenario one) uptake was already high and steadily declined or whether (scenario two) it showed a wave of increase and decrease corresponding to usage of leaded gasoline (e.g. compare Nevin, 2000 vs. McCall and Land, 2004).

In order to retrospectively distinguish between these scenarios, and in the absence of reliable PbB data before the 1970s, lead concentrations were determined in permanent tooth enamel as a measure of exposure and uptake. Teeth were obtained from mostly African-American adults who grew up in the Cleveland area and whose molars were formed from about 1936 to 1993. Core enamel in adult teeth preserves virtually unchanged the record of both childhood lead exposure and childhood ratio of lead isotopes throughout an individual's life (Gulson et al., 1997; Gulson and Gillings, 1997). Next, since continuous national measurements of atmospheric lead were unavailable until the mid-1970s (US EPA, 1986), the temporal changes in teeth enamel lead were compared to two different proxies of historic atmospheric exposure: lead in two dated Lake Erie core sediments, and national data on lead consumption in gasoline (US Bureau of Mine, 1941-1990; Nriagu, 1990), which is closely correlated with atmospheric lead (Figs. 5–7 in US EPA, 1986). In addition, since PbB is the most widely used metric to relate lead burden to toxic effects, a correlation was sought between lead in teeth and reported values of PbB during the phase-out of leaded gasoline, in order to estimate the peak PbB at the time of peak lead in teeth.

Finally, it was determined whether values and changes of $^{207}Pb/^{206}Pb$ isotope ratios of molar tooth enamel formed in the years 1936–1993 were consistent with those of atmospheric lead found in the dated Lake Erie sediment cores. Ratios of lead isotopes from different sources (e.g. paint, industrial, leaded gasoline) may have source-characteristic values depending on both the predominant mining or recycling sources at the time, and the relative abundance of such sources in the samples analyzed (Gulson et al., 1997; Gulson and Gillings, 1997).

In a similar vein, Farmer et al. (2006) correlated lead isotopic ratios in teeth sections and in sphagnum moss (as an indicator of atmospheric lead) in materials collected in Scotland over 100 years. However, as the authors pointed out, the temporal resolution was constrained by the limitations of teeth samples containing dentine, which integrates life-long rather than just childhood exposure to lead. They recommended use of core tooth enamel, as employed here. In addition, Scotland apparently experienced relatively much more pre-gasoline industrial lead atmospheric exposure than reported in the US (Farmer et al., 1996).

2. Methods

2.1. Tooth and donor characteristics

Mandibular and maxillary first and second molars, extracted strictly for reasons of dental necessity, were obtained with the cooperation of the Northeast Ohio Neighborhood Clinics and The Free Clinic of Greater Cleveland. Donor consent and information preserving anonymity were obtained according to a protocol reviewed and approved by the Case Western Reserve University Institutional Review Board. Tooth donors were 10 years of age or older, and grew up at least from ages 2 to 5 years (when the first molar was 50% formed) or 5 to 9 years old (second molar 50% formed) in "Greater Cleveland" (the city of Cleveland and surrounding mostly urban suburbs). The questionnaire accompanying each donated tooth included; donor age, sex, ethnicity/race, and name of the neighborhood (standardized within the City of Cleveland as so-called "statistical planning area", or using name of suburb) in which the donor resided during the donor's years of permanent molar formation.

During the years 2001–2003, 127 non-duplicate tooth samples were obtained in which both lead concentration and lead isotope ratios were measured, covering the years of tooth formation from 1936 to 1993. Three of these samples were deleted from the results as outliers because lead concentration levels were more than five-folds greater than the mean of other data values in similar years. These exceptionally high values may have resulted from unique intense environmental lead exposures (e.g. from greatly deteriorating lead-painted housing, proximity to lead-battery recycling plants, etc.) or inadvertent inclusion of high lead superficial surface enamel (Budd et al., 1998). The latter explanation is more likely because these teeth values, if real, would have been equivalent to PbB values of around 200 μg/dl (see Results), which would have been fatal or disabling. The 124 included samples consisted of 60 first and 64 second molars obtained from 59 males, 63 females and 2 with no information as to the sex. Ethnicities included 107 African-American, 16 Caucasian and 1 unknown. Because African-American tooth donors comprised 86% of this sample, comparisons between the tooth and national blood data were made using data from African-American children. Of the 124 tooth donors, 108 were raised in the Eastern half of the City of Cleveland, 5 in the Western half, 9 in surrounding suburbs, and 2 in unrecorded locations in the same county. For most analyses of the temporal change in tooth lead and its correlation with surrogates of atmospheric lead, individual data points were used without reference to neighborhood of origin. However, for the multivariate regression analysis, where neighborhood was a covariate of interest, data from neighborhoods with fewer than 4 data points (with one exception) were clustered into a set of neighborhoods that were contiguous or shared similar traversing and adjacent major traffic routes. The exception was a neighborhood with unique traffic routes and $n = 3$.

An association of dental caries with elevated tooth lead concentration, reported in deciduous teeth (e.g. Tvinnereim et al., 2000), was found to be weak or non-existent in permanent teeth (Campbell et al., 2000; Gemmel et al., 2002; Youravong et al., 2006), which were used in this study. Therefore, the use of very carious teeth (requiring extraction) did not necessarily select for teeth with high enamel lead. Further, if such selection existed, there would have been a deviation from the observed strong linear correlation between tooth lead and blood lead levels reported nationally (see Fig. 3, Results).

2.2. Local environmental exposures to lead of donor population

2.2.1. Housing

Based on year 2000 County Auditor data on the age of housing in the different city neighborhoods and suburbs (Center for Community Solutions and United Way Services, 2004), the percentage of housing built on or before 1960 was calculated for the neighborhood of each tooth donor as the percentage of total structures built until 1991 (data after 1991 were excluded because of an intense housing construction program). In the recorded childhood neighborhoods of 122 tooth donors (excluding the 2 donors with unrecorded childhood neighborhoods), the median percentage of housing structures built on or before 1960 in 1991 was 93%. In other words, in the period of interest between 1936 and 1993, most tooth donors lived in pre-1961 homes with significant lead paint hazards (Weaver, 1989; President's Task Force, 2000; Jacobs et al., 2002). In Cleveland, urban renewal was not a major factor in the lead uptake of the tooth donors in this study. Only about 20% of donors grew up in neighborhood clusters in which 27–40% of the housing dated from 1960 or later, whereas 69% of donors grew up in neighborhoods in which less than 20% of the housing was built in 1960 or later.

2.2.2. Traffic

Auto traffic in the Cleveland donor population area might also affect lead exposure. An estimate of relative average total daily weekday traffic (Tues–Thurs) in Cleveland, on key state roads and including later interstate highways, was supplied by the Ohio Department of Transportation (personal communication) for multiple years from 1948 to 2000. For each neighborhood (or neighborhood cluster), the average daily traffic counts for the years 1960–1980 (peak period of leaded gasoline usage) was computed, and then weighted by the number of tooth donors in that neighborhood.

2.2.3. Other exposure sources

Another source of exposure was atmospheric lead emission from coal or ore smelting, which apparently reached a maximum around 1910, after which it was more or less constant at least until 1985. Still, peak emission from leaded gasoline was about 40 times greater than either of these sources (Graney et al., 1995). Finally, although no water analyses are available prior to 1993, drinking water was not likely to be a major source of lead intake. Cleveland water is moderately hard and has a pH of 7.0–7.6 so that it does not tend to dissolve lead in household pipes (Cleveland Division of Water, 2007). Although most of the population's household plumbing was originally lead, over time this tends to become covered with insoluble lead carbonate scale and hence releases less lead into the drinking water (e.g. Sharrett et al., 1982). Also, the water system's lead connector pipes were replaced in the 1950s and in 1992, the earliest date of household analyses, 4 out of 29 households in the city of Cleveland exceeded 15 μg/liter (Cleveland Division of Water, personal communication). At these lead levels, drinking water would not have contributed greatly to lead burden (Lanphear et al., 1998).

2.3. Designation of age of enamel formation in human molars

To facilitate statistical analysis, it was necessary to assign a single year to each tooth as the approximate year of 50% crown enamel formation (not full eruption) based on each donor's birth date. Although studies of enamel formation in the first and second permanent adult molars give differing results (Simpson and Kunos, 1998), those of Simpson and Kunos (1998) were used here to assign ages for enamel development because: all the permanent teeth in their study were from the Cleveland area; they used careful radiologic data and multiple grades of enamel formation; and because one could estimate a 50% enamel completion date directly from their Figs. 12 and 13 (approximately ages 2 and 6 for first and second molars, respectively). It is clear from these figures that enamel formation is non-linear with time, and that the age of 50% enamel completion varies +/−1 year from the central estimate used here.

2.4. Processing and analysis of tooth enamel

The extracted tooth was stored in 10% formalin phosphate solution, which tests showed contributed a negligible (<1%) fraction of the total lead content later found in the enamel. Next, the tooth was removed and rinsed thoroughly with distilled water. The outermost surface was cleaned with a medium grit diamond burr (#856, Brasseler USA Dental Rotary Instruments), removing an estimated 15–30 μm of enamel, and any remaining decay was removed with a round carbide burr (#4, 6, and 8). Because in most cases, the molars had been extracted due to extensive decay, remaining enamel (usually a thick region of healthy enamel on a marginal ridge or remaining cusp tip) was taken wherever it was available within the tooth. Using 3.3× magnification to isolate, access and visualize the dentin-enamel junction, the dentin was completely removed, leaving a clean sliver of enamel projecting from the underlying tooth structure. The enamel sliver was snapped off, rinsed with distilled water, and stored dry in a sterile container until chemical analysis.

Tooth dissolutions were carried out in a biological safety cabinet with HEPA-filtered air to minimize atmospheric lead contamination. Polypropylene sample containers were pre-cleaned with dilute trace metal grade nitric acid solution. Enamel specimens were weighed into pre-cleaned sample containers, and were surface-cleaned with a 60 s treatment with 1.6 M aqueous nitric acid to further minimize contaminants or surface layer lead. The etching process was evaluated in trial dissolution experiments to determine the approximate percent mass loss and resulting thickness of enamel removed. Five dry, weighed fragments of enamel (density 2.9 g/cm^3) were etched by soaking in 1.6 M HNO_3 at 20 °C for 60 s; thereafter, the enamel sample was rinsed thoroughly with deionized water and dried to constant mass. Enamel fragments lost about 14% of their mass through this treatment. When the enamel fragment was modeled as a cube, the pre-etch and post-etch dimensions of the enamel fragment could be calculated. This calculation revealed that the enamel thickness lost was 67 ± 17 (SD) microns. The calculated thickness lost was in reasonable agreement with digital micrometer measurements made before and after the 60 s etching treatment. Thus, the combination of mechanical abrasion and acid etching removed from 82 to 97 μm of surface enamel.

In teeth used for further analysis, the acid was removed and the tooth was rinsed twice with deionized water, dried at ambient temperature, weighed, and dissolved in 1.6 M aqueous nitric acid. An aliquot of the tooth solution was used to determine lead concentration by an isotope dilution procedure in which NIST 983 (Radiogenic lead, 92% ^{206}Pb) was used as the source of the lead spike. The relative uncertainties in lead concentration were approximately 1%, as determined by RMS propagation of the precision of the unspiked and spiked sample ratio results.

The remainder of the solution was used to measure lead isotope composition, measured by inductively coupled plasma mass spectrometry (ICPMS) using a VG PQII quadrupole ICPMS or a VG Axiom MC sector ICPMS. Because of the relatively low sample lead concentration, the VG Axiom MC was used in the single collector (electron multiplier) mode. The isotopic data quality was evaluated using NIST 981 (Common lead) as a control sample. Tl was added at 2 μg/L to correct for mass discrimination effects (Ketterer et al., 1991). The uncertainties in the lead isotope ratios, ^{207}Pb/^{206}Pb and ^{208}Pb/^{206}Pb, were estimated at approximately 0.5% relative as derived from the root mean square of the sum of a precision term (relative standard deviation) plus the bias (relative percent difference between observed and certified values).

2.5. Lake Erie coring, dating, and sediment analysis

Data from two Lake Erie cores were incorporated in this study: one reported by Graney et al. (1995), and the other, designated here as the

"new core", collected in July 2002 from the Lake Erie Central Basin 35 km northwest of Cleveland. Published Pb concentrations and isotopic data from the Graney et al. (1995) core data obtained in 1991 were chosen for use here because of the relatively large number of published data points dated 1936 to 1992 (spanning most of the history of leaded gasoline usage per Nriagu, 1990), whereas no single dated Lake Erie core in other available studies (e.g. Nriagu et al., 1979; Ritson et al., 1994) encompassed these years. Also, the choice to use this data set was made before teeth data were available. The "new core", obtained by Prof. Gerald Matisoff et al. (Case Western Reserve University, Department of Geological Sciences), was collected for purposes unrelated to this study. Since prevailing winds in Cleveland are mainly from the south, southwest and west (Bolsenga and Herdendorf, 1993), the new core location would be partially downwind to some of Cleveland atmospheric emissions (as would the lake core used by Graney et al., 1995). The "new core" was obtained with a 6.5 cm i.d. gravity corer, equipped with a plastic insert for the retrieved core, was extruded and sliced into appropriate intervals of 0.5, 1.0, or 2.0 cm. Sediments were dried at 60 °C for 48 h and then ground with an alumina mortar and pestle. The chronology of this core was determined by ^{137}Cs and $^{239+240}$Pu dating procedures (Ketterer et al., 2000; Ketterer et al., 2002) based on three definite dates: 2002, 1963, and 1952. The 1952 date corresponds to the first detection of synthetic ^{137}Cs and $^{239+240}$Pu in nuclear weapons testing debris in Northern Hemisphere, and the 1963 date coincides with the maximum deposition of stratospheric fallout (Ketterer et al., 2002). The uncertainty associated with these dates is 1952 ± 2 and 1963 ± 1, respectively. All other dates were inferred by interpolation and extrapolation of these three markers.

To determine lead concentration in Lake Erie sediments, ~100 mg sediment subsamples were completely dissolved with 1 mL each of HF and HNO_3. After addition of excess boric acid to neutralize HF, samples were diluted to 50 mL and lead concentration was determined by ICPMS in a diluted aliquot. The "total dissolution" procedure was used in the analysis of lead concentration in the 2002 "new core", as it was considered important to obtain an accurate measure of the total concentration of all lead components in the sample, including both naturally occurring alumniosilicate as well as anthropogenic lead.

In contrast, lead isotope ratios were measured in acid-leached sediment aliquots in an attempt to preferentially measure the more relevant anthropogenic pollution component of the sediment lead. For this purpose, solutions were prepared by leaching ~100 mg sediment samples with 5 mL 16 M HNO_3. The sample solution was diluted to 50 mL volume and lead was isolated from the sample solution using 50 mg columns of a selective extraction resin (Pb-Spec, Eichrom, Darien, IL), which concentrates lead from the 1.6 M HNO_3 solution. After column rinsing with 1.6 M HNO_3, lead was eluted with 2 mL of 0.05 M ammonium oxalate solution. Finally, lead isotopes were determined using the VG Axiom MC instrument operating in the multiple collector mode. Uncertainties of about 0.01% relative difference were obtained for the ratios ^{207}Pb/^{206}Pb and ^{208}Pb/^{206}Pb.

2.6. Comparisons of data analysis and characteristics of the two lake core sediments

Various researchers have attempted to calculate the "anthropogenic" lead concentration in sediments and to distinguish the isotopic composition of the added "anthropogenic lead" from the measured lead isotopic composition of the (anthropogenic + background) lead. For example, Shirahata et al. (1980) and Graney et al. (1995) used

$$\left(^{207}\mathrm{Pb}/^{206}\mathrm{Pb}\right)_{\mathrm{anthropogenic}} = \frac{\left(^{207}\mathrm{Pb}/^{206}\mathrm{Pb}\right)_{\mathrm{total}} * (\text{ppm total Pb}) - \left(^{207}\mathrm{Pb}/^{206}\mathrm{Pb}\right)_{\mathrm{background}} * (\text{ppm background Pb})}{\text{ppm total Pb} - \text{ppm background Pb}}$$

to calculate the concentration and isotopic composition of the added "anthropogenic-only" lead component. However, with the data available here, $(^{207}\mathrm{Pb}/^{206}\mathrm{Pb})_{\mathrm{anth}}$ could not be determined within any meaningful error constraints due to the unavoidable, relatively large uncertainties of ~5% relative in lead concentration$_{\mathrm{total}}$. Moreover, even if more precise lead concentration$_{\mathrm{total}}$ measurements could be attained by isotope dilution methods, the true errors in lead concentration$_{\mathrm{total}}$ would still be constrained by sample homogeneity and errors associated with sectioning of the core into individual strata. For these reasons, $(^{207}\mathrm{Pb}/^{206}\mathrm{Pb})_{\mathrm{total}}$ rather than $(^{207}\mathrm{Pb}/^{206}\mathrm{Pb})_{\mathrm{anth}}$ was utilized. As a result, the measured $(^{207}\mathrm{Pb}/^{206}\mathrm{Pb})_{\mathrm{total}}$ contains a relatively constant addition from the background (^{207}Pb/^{206}Pb), but this addition should not affect interpretation of the relative trends in $(^{207}\mathrm{Pb}/^{206}\mathrm{Pb})_{\mathrm{total}}$ vs. time.

Differences in lead temporal profiles and isotope composition (see Results) might be expected in the two different lake core data sets. First, Graney et al. (1995) utilized an acid leaching procedure, which did not dissolve all lead present in aluminosilicates, while the "new core" sediment was totally dissolved, adding slightly more lead to the non-anthropogenic lead baseline. Second, the "new core" was collected from the Central Basin whereas Graney et al. (1995) sampled the Eastern Basin. Based on previous comparisons of Central and Eastern basins, the "new core" data is expected to reflect greater mixing of inflowing sediment (70% vs. 29%, Ritson et al., 1994), as well as slower sedimentation rate and substantial input from the Detroit River and from municipal waste discharges (Nriagu et al., 1979). Probably for these reasons, the time course of the Graney et al. (1995) lead data was more in accord with national data on lead incorporation into gasoline (see Results, Fig. 2). Thus, the "new core" data was used mainly for overall confirmation.

2.7. Equivalence of data with isotope ratios, ^{207}Pb/^{206}Pb and ^{208}Pb/^{206}Pb

Based upon lead isotope systematics, highly significant correlations are expected between ^{207}Pb/^{206}Pb and several other ratios (e.g. ^{208}Pb/^{206}Pb). Since many previous studies have used the ^{207}Pb/^{206}Pb ratio (or its inverse), this ratio was chosen to report in the present results. However, corresponding trends were obtained using ^{208}Pb/^{206}Pb ratios: $R^2 \geq 0.9$ were found between ^{208}Pb/^{206}Pb and ^{207}Pb/^{206}Pb ratios for tooth and lake sediment data. Of all the various isotope ratios, the ^{207}Pb/^{206}Pb ratio exhibited the smallest relative error in both tooth and sediment data, as expected because of the greater abundance of these two isotopes.

2.8. Estimation of lead consumed in US gasoline production, 1937–1990

Data on total lead consumed as an additive to gasoline are available for 1941–1986 (US Bureau of Mine, 1941-1990). All data were converted to metric tons. After 1986, the Bureau of Mines included leaded gasoline additives in the category "miscellaneous uses" "to avoid disclosing company proprietary information". To estimate the amount of leaded gasoline additives consumed from 1987 through 1990, it was assumed that the "miscellaneous" category in 1986, which in that year did not include leaded gasoline additives, was constant from 1987 through 1990, and that thereafter the total of "miscellaneous" additives minus the tons of "miscellaneous" in 1986 was the amount of leaded gasoline additive in those years. Also, The Bureau of Mines 1991 yearbook stated that leaded gasoline production ceased in 1990, so the value zero was adopted for 1991 and later. Data for the years 1937 through 1940 were taken from Fig. 1 in Nriagu (1990).

2.9. Statistical analyses

An array of parametric and nonparametric statistical procedures was applied to statistically evaluate the two scenarios presented in the Introduction. Since tooth samples included both first and second

molars, a new nonparametric curve testing procedure, allowing for heteroscedastic error variances, was developed (Zhang, 2005) to test if there were significant differences in lead concentration over the years between these two data sets, whose variances were unequal. The non-significant result (at a global significance level alpha = 0.05) meant that it was reasonable to pool the tooth results of first and second molars and relate the "response variable", tooth lead concentration, to other "human covariates" (the year of 50% enamel formation, sex, race, and neighborhood in which the donor lived during enamel formation) as well as the "non-human environmental covariate", lead concentration in Lake Erie core data. Temporal trends in tooth lead isotope ratios were also analyzed with respect to changes in lake core sediment isotope ratios.

2.9.1. Tooth and lake sediment lead concentrations

The mean curve of lead concentration in teeth and in Lake Erie cores over the years of this study was estimated using a cubic smoothing spline (a nonparametric procedure used to fit an arbitrary smooth curve) with the degrees of freedom set at 6 (per S-Plus 8 Guide, 2007). The corresponding lead concentration curves from the two Lake Erie cores were approximated by simple interpolation between data points because of the small sample sizes (11 from the Graney et al. (1995) core, 17 from the new core data, vs. 124 tooth samples) and the much less confounded variances than those of the tooth data.

2.9.2. Analysis of isotope ratio data

Since lake samples were not available in all of the years in which the molars (in the tooth data) were 50% formed, values for the missing data were imputed using linear interpolation between data points from the lake sediment.

3. Results

3.1. Lead in tooth enamel and surrogates of atmospheric lead

Using date of birth and estimated age at half-maximal enamel formation in first and second molars, as well as smoothing techniques (see Methods), trends in tooth enamel lead concentration were plotted from 1936 to 1993 (Fig. 1). These data show a unimodal increase and later decrease in lead uptake over these years, as predicted in Scenario two (see Introduction). The peak smoothed value of tooth lead (4.94 μg/g) was about five-fold (and significantly) greater than the average value in the ascending and descending years (1936–1950 and 1986–1993, respectively). The scatter in tooth lead values is considered in the Discussion.

Given the unimodal curve observed in Fig. 1, the next step was to test whether changes in tooth lead corresponded to those in the surrogates of atmospheric lead. Before doing so, it was important to evaluate which one(s) of the surrogates was most indicative of atmospheric lead. In fact, regression analysis between lead consumed in gasoline production and the time course of lead concentration in the two lake sediments

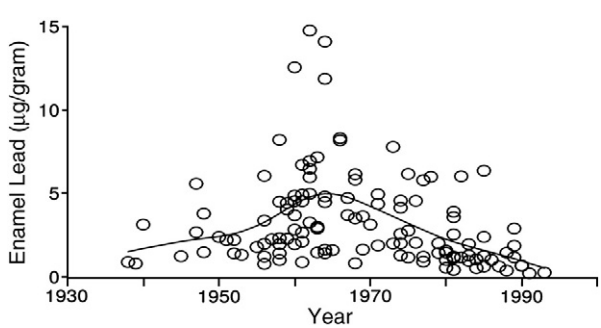

Fig. 1. Concentration of lead in tooth enamel at year of 50% enamel completion, 1938–1993.

Table 1
Regression relation between lead consumed in US leaded gasoline production and lead concentration in Lake Erie sediments.

Regression of lead consumed in US production of leaded gasoline with:	Coefficient	Standard error	Adjusted R^2	*p*-value
Graney et al. (1995) lake sediment	4.5884	0.2269	0.77	<0.00001
New core lake sediment	2.0992	0.2504	0.37	<0.00001

(Table 1) showed significant correlations with both lake sediments. However, the Graney et al. (1995) sediment values accounted for 77% of the variation in gasoline lead while the "new core" accounted for 37% (see R^2 values, Table 1). Therefore, results with Graney et al. (1995) lake sediment were considered the better lake sediment surrogate for atmospheric gasoline, probably for both methodologic and locational reasons (see Methods and Discussion).

If the unimodal time course of tooth lead levels reflected exposure to atmospheric lead due to gasoline, there should be good correlation between the temporal sequence of tooth lead levels with those of lake sediments and lead consumption in gasoline. This was observed graphically (Fig. 2). The two Lake Erie cores give somewhat different profiles before and after the peak years, with a persistent higher lead concentration during the phase-out years in the "new core". Relative tooth lead values correspond most closely to the Graney et al. (1995) lake sediment values, although with a somewhat earlier decline.

Statistically, univariate log-linear regression of lead concentration in teeth vs. that in Graney et al. (1995) lake core sediments and in leaded gasoline production provided better fits than their counter parts without the logarithm transformation, respectively, yielding moderate R^2 values (0.33 and 0.26) and significantly non-zero regression coefficients β (Table 2). The regression with "new core" lake sediment produced poor R^2 values with marginally significant non-zero regression coefficients β with log transformation but significant (but still low R^2) without log transformation. The unusual shoulder of the phase-out stage of the "new core" sediment (see Discussion) probably accounts for this poor R^2 value compared to that of the Graney et al. (1995) lake core sediment.

As explained in Methods, the dating of both 50% tooth enamel formation and of the lake cores had an uncertainty of respectively +/−1 and ~2 years, respectively. Also, the two lake core peaks of lead concentration were shifted slightly to the right of the tooth peak (Fig. 2). Therefore, a series of tests were run to determine the sensitivity of the correlation between teeth and sediment lead concentration trends to shifts of dating of either enamel formation or lake sediment (using the Graney et al., 1995 lake core data). The result showed maximal correlation between the two data sets in an interval of 0 to 3 years, with a confidence of 95%. Since the shift of zero years cannot be ruled out, no time-shift transformation was used in the analyses.

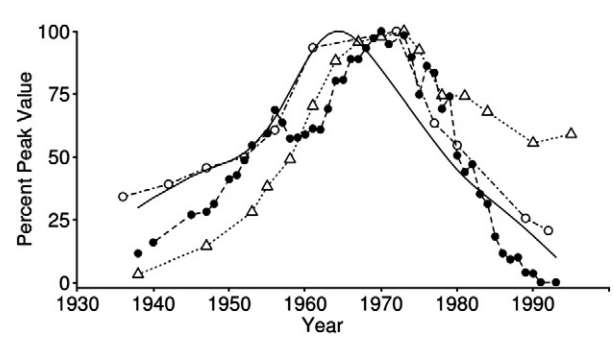

Fig. 2. Comparison of relative temporal changes in lead concentration in tooth enamel and lake sediments, and relative changes in the total amount of lead additives to gasoline. Maximum absolute values and symbols are: 4.94 μg/g (teeth, smoothed data, uninterrupted line), 72.7 ppm ("new core Lake Erie sediment, triangles), 41.1 ppm (Graney et al., 1995 Lake Erie sediment, open circles), and 253,000 mt of lead additives to gasoline produced in the US, closed circles (see Methods).

Table 2
Regression relationship between lead concentration in tooth enamel and that of Lake Erie core sediments, or lead consumed in production of leaded gasoline.

Regression of log (lead concentration in tooth enamel) with:	Coefficient β	Standard error	R^2	p-value
Log (Graney et al. 1995 lake sediment)	0.9886	0.1269	0.33	<0.00001
Log (new core lake sediment)	0.2144	0.1259	0.02	0.091
New core without log transformation	0.0311	0.0123	0.05	0.0132
Log (lead consumed in leaded gasoline production)	0.3183	0.0487	0.26	<0.00001

3.2. Multivariate analysis

The moderate R^2 values (0.33 and 0.26) found in the univariate regression (Table 2) indicate that other factors contributed to the variation of lead in teeth. In order to elucidate these factors, a variety of possible models was examined and a step-wise regression was performed from each of these. The best model relating lead concentration in tooth enamel to all the covariates we had available (Eq. (1)) accounts for 53% of the total variation for tooth lead (Table 3) and was highly significant (p<0.00001). The model was of the form:

$$\mathrm{Ln}(\mathrm{Tooth}[\mathrm{Pb}]) = \alpha + \beta{*}\mathrm{sex} + \beta_2{*}\mathrm{race} + \beta_3{*}\mathrm{nbhd} + \beta_4{*}\mathrm{Ln}(\mathrm{GrPb}) + \gamma_1{*}\mathrm{race}:\mathrm{nbhd} + \gamma_2{*}\mathrm{sex}:\mathrm{Ln}(\mathrm{GrPb}) + \varepsilon \quad (1)$$

where Tooth [Pb] is the lead concentration in the tooth enamel, coefficient α represents the intercept, β_i's are the coefficients for the main effects, nbhd is neighborhood or neighborhood cluster in which the tooth donor lived as a child, GrPb is Graney et al. (1995) lake sediment lead concentration, γ_i are the coefficients for the interaction terms, and ε represents remaining unexplained sampling or random error. As noted in Methods, some "neighborhoods" were clusters of adjacent Cleveland "Statistical Planning Areas" and/or suburban cities, sharing similar traffic routes. All such clusters were made prior to the regression analysis.

By far, the most significant covariate was the (Graney et al., 1995) lake sediment lead concentration (on a logarithmic scale). To a lesser extent, there were 5 neighborhoods with significant coefficients (p<0.05), some also showing negative interaction with Caucasian race, and one interaction of male sex and lake sediment lead concentration.

While the correlation with the atmospheric surrogate (Graney et al. lake sediment) is expected from the previous results, the significant neighborhood covariates were further analyzed. As noted in Methods, neighborhoods were clustered if the number of tooth data per individual neighborhood was less than 4 and the neighborhoods were adjacent to or traversed by similar major traffic routes. In fact, 4 of the 5 significant neighborhoods were exposed in 1960–1980 to traffic on major routes with 26,000 or more cars per day, whereas 5 of the 7 non-significant neighborhoods had less than 26,000 cars per day. The median traffic was 72,000 cars per day for the significant and 20,000 for the non-significant neighborhoods. Therefore, extent of traffic during the peak use of leaded gasoline appears to be an underlying element emerging from the multivariate regression analysis.

Age of housing might also influence neighborhood data because of much greater use of lead in paint prior to the 1960s (Weaver, 1989; President's Task Force, 2000; Jacobs et al., 2002). However, the weighted median percent of homes built in or before 1960 (see Methods, including qualifications) was similar in the "significant" and "non-significant" neighborhoods (84% and 82% respectively). As explained in the Discussion, this finding in no way excludes leaded paint in housing as an important ongoing source of childhood lead uptake during the period in question. Indeed, since our data do not contain the detail of the age or condition of the particular home(s) in which the tooth donor grew up, the neighborhood-level housing data provide only a broad indication of childhood lead exposure due to paint.

Lastly, there were 3 neighborhoods that showed negative coefficients when interaction with Caucasian race was included. These results fit with those of national studies on PbB which consistently show greater PbB in black than in white residents of the same communities.

Although the trend in enamel lead uptake from 1936 to 1993 follows the exposure to leaded gasoline, the relative amount of lead uptake due to leaded gasoline as opposed to that from other sources (mainly deteriorated house paint as well as leaded food cans, industrial emissions, etc.) needs to be determined. This source apportionment was estimated by assuming that the area under a line extending from the 1936 "baseline" enamel Pb to the 1993 level (Fig. 1 or 2) was proportional to pre-existing and declining non-gasoline exposure. Since no substantial new sources of lead exposure other than leaded gasoline are known for this time period, the remaining area of enamel Pb above the pre-existing level was assumed to be due to exposure to leaded gasoline. The latter area comprised 63% of the total area under the smoothed tooth enamel curve, and conversely the pre-existing and continuing baseline exposure amounted to 37%. Since by 1930, some leaded gasoline was already being manufactured (Nriagu, 1990) and was already contributing to atmosphere lead, as observed in Lake Erie sediments (Graney et al., 1995), the baseline (37%) percentage is an overestimate of non-gasoline sources, because in 1936 it would include some uptake due to low levels of leaded gasoline. In addition, the baseline exposure is assumed to be linear, whereas urban renewal in some neighborhoods (see Methods) and phase-out of soldered food cans (see Introduction) may have accelerated the decline in non-gasoline related lead sources. Therefore, a conservative summary of this result would be that from 1936 to 1993, gasoline lead accounted for about two-thirds of total childhood lead uptake.

Table 3
Results of multiple regression analysis of log (enamel lead concentration) with covariates log (Graney et al., 1995 lake sediment lead concentration), gender, race, and neighborhood.

Covariate	Coefficient	Standard error	Probability (>|t|)
(Intercept)	−4.3350	0.7729	<0.00001
Log (Graney et al. lake sediment lead conc.)	1.1798	0.1784	<0.00001
Nbhd 1	1.5779	0.7429	<0.05
Nbhd 2	1.6060	0.7269	<0.05
Nbhd 3	1.5635	0.7374	<0.05
Nbhd 4	1.6939	0.7120	<0.05
Nbhd 5	1.4467	0.7176	<0.05
Nbhd 6	1.3338	0.7635	0.05<p<0.1
Nbhd 7	1.2113	0.7215	0.05<p<0.1
Nbhd 2: Caucasian race	−2.3993	1.1301	<0.05
Nbhd 4: Caucasian race	−2.4558	1.1160	<0.05
Nbhd 5: Caucasian race	−3.0600	1.1107	<0.01
Male gender	0.9637	0.8695	0.05<p<0.1
Male gender:log(lake sediment lead conc.)	−0.5894	0.2643	<0.05

Residual standard error: 0.6688 on 96 degrees of freedom; Multiple R-Squared: 0.53, p-value <0.00001. Results for covariates where p>0.1 are not included.

3.3. Correlation between observed tooth lead and reported national blood lead levels, and extrapolation to peak PbB

The most common measure of population lead uptake is PbB. In order to determine whether the present results in teeth are consistent with US nationally reported results of PbB, the observed tooth lead concentration at points during the phase-out period was compared to those in 3 available reports of blood lead concentration in comparable populations of urban African-American children at the same time periods (Fig. 3, see caption for detail). The result (Fig. 3) must be regarded as an approximation because the reported data on blood levels: a) had confidence limits of 5–10%; b) subsumed ages 0.5 to 5 years, even though in any given year, there was a decline in PbB with

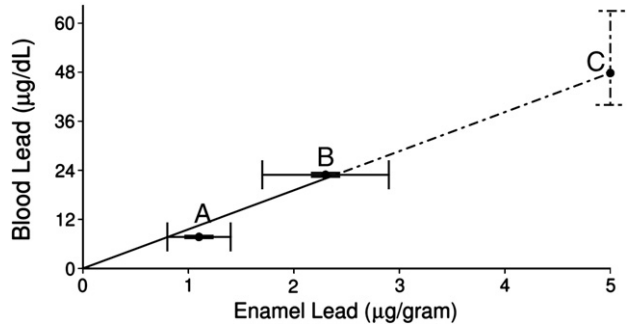

Fig. 3. Correlation of observed tooth lead values and reported population PbB values, assuming passage through the origin. Blood data were for African-American children 0.5 or 1 to 5 years of age, reported in national studies (years covered given in parentheses): A. Brody et al. (1994) (1988–1991), African-American children in cities over 1 million population; and B. Mahaffey et al. (1982) (1976–1980), African-American children in "central cities". Point C is the extrapolated value of PbB obtained by using the maximum smoothed tooth lead of 4.94 µg/g (as in Fig. 1) and a least square linear equation. Data ranges for PbB and enamel lead for points A and B are the mean and SEM (standard errors of the mean). Note that the range for SEM of the enamel data at points A and B (+/−0.3 and 0.5, respectively) is similar to the size of the closed circle data points. For point A, mean and SEM of PbB were based on pooled variances computed from the published confidence intervals (Brody et al., 1994), assuming that the data were log-normal distributed. For point B, mean and SEM of PbB were found by pooling variances from the two published SEM's (Mahaffey et al., 1982). The range of extrapolated PbB values for point C was found as explained in the text.

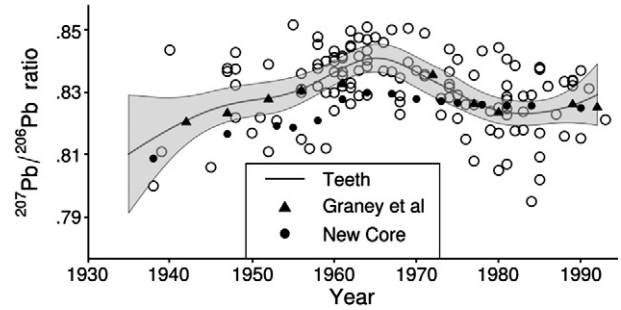

Fig. 4. ^{207}Pb/^{206}Pb isotope ratios in teeth and lake sediments during the course of leaded gasoline introduction, peak, and phase-out. The line and shaded area for tooth isotope ratios is the smoothed average +/−one standard error, and the open circles are individual tooth data points. The error bars on the individual lake sediment data points (not shown) were approximately the same size as the symbols.

age, and the enamel of 2nd molars used (about half the sample in this study) was half formed only at 6 years; c) included years within which PbB at any given age was declining, and within which there were seasonal variations; and d) included children with different income levels and ages of housing, which affect lead levels. On the other hand, tooth enamel lead concentration integrates over 3–4 years some of these variations in exposure. In any event, in contrast to other reports (Fergusson and Purchase, 1987), and in agreement with results from whole deciduous teeth (Rabinowitz, 1995), a strong correlation was found (R^2 ranging from 0.92 to 0.99 depending on errors of measurement explained below) between lead in tooth enamel and reliable PbB data in comparable years (Fig. 3). Given this correlation, the maximum value of the smoothed tooth data was used in a linear regression to find an extrapolated peak PbB for the years 1960–1975. In order to estimate the error range of this extrapolated peak, a range of 8 slopes were derived (for points A, B, and C, Fig. 3) using at least one of the enamel lead errors and fixed mean blood data, yielding an extrapolated PbB ranging from 40.0 to 63.5. On the other hand, when 8 slopes were derived (for points A, B, and C, Fig. 3) keeping mean enamel lead fixed and adding or subtracting PbB errors, the extrapolated PbB ranged from 46.7 to 48.9. Therefore, using the wider range of error, the extrapolated mean PbB for the years 1960–1975 was 47.8 with an error range of 40.0 to 63.4 (C, Fig. 3).

3.4. ^{207}Pb/^{206}Pb isotope ratio in tooth enamel and Lake Erie cores

If atmospheric lead in the peak years was the dominant source of exposure in urban Greater Cleveland children, ^{207}Pb/^{206}Pb in tooth enamel should follow similar trends to those of ^{207}Pb/^{206}Pb in Lake Erie sediments at least during the peak years.

In the entire period 1993–2003, the absolute values of Graney et al. lake sediment ^{207}Pb/^{206}Pb were within the 95% confidence limits of teeth ratios (Fig. 4), while those from the "new core" were largely parallel but mostly less than those from teeth. This finding is consistent with the observed lead profiles (Fig. 2) and regression analyses (Table 2), in that the Graney et al. (1995) lake sediment data more closely tracked the data on lead added to gasoline than did the "new core".

The trends in ^{207}Pb/^{206}Pb were similar between teeth and sediment (Fig. 4). Linear regression analysis, in agreement with Fig. 4, showed significant positive associations between isotope ratios of tooth and respective lake sediments. As expected from lead concentration results (Table 2), the agreement of tooth ^{207}Pb/^{206}Pb with trends in Graney et al. (1995) lake sediment ($R^2 = 0.23$, coefficient significant at $p < 0.0001$) was better than with the "new core" sediment ($R^2 = 0.11$, coefficient $p < 0.0002$). Also, as expected, ^{208}Pb/^{206}Pb ratios (not shown) were closely correlated to ^{207}Pb/^{206}Pb ratios, and displayed similar trends.

4. Discussion

4.1. Sources of variation in tooth data

Many factors probably increased the variation in the tooth data. As noted in Methods, the age at 50% first or second molar enamel formation varies between individuals by 2 years, and varies in different reports (Simpson and Kunos, 1998). However, a shift analysis showed that a deviation of 2–3 years in the assigned single "age" of 50% enamel formation would not have substantially changed the observed correlation between trends in lead concentration of teeth and that of Graney et al. (1995) lake sediment.

The fact that tooth lead values obtained during the phase-in or phase-out of leaded gasoline integrate over years when lead exposure was either increasing or decreasing, adds additional variation. Also, based on PbB studies, an additional two-fold variation apparently depends on family income, and another 1.5 fold because PbB is higher in 1–2 year olds than in 3–5 old children (Pirkle et al., 1998), i.e. during early and late ages, respectively, of enamel formation of permanent molars.

Lead concentration within the enamel declines steeply in the first 30 µm between the surface and the core (Purchase and Fergusson, 1986; Fergusson and Purchase, 1987; Budd et al., 1998). The method of tooth preparation used in this study removed about 80 to 100 µm of surface enamel with its high lead concentration. This amount of removal was similar to that of Budd et al. (2000) and Budd et al. (2004), where "over 100 µm" of surface enamel was removed in order to confine analysis to "core enamel". Still, non-homogeneous lead concentration within the core enamel would tend to increase variation in the data.

In sum, the many variables contributing to tooth lead values would greatly increase the chance of missing overall trends and finding correlations between tooth data and other variables, but in fact significant correlations were found.

4.2. Lake core data — qualifications

Dated aquatic sediments have often been used to reconstruct past environmental trends in atmospheric and aquatic pollutants such as lead (e.g. Graney et al., 1995; Renberg et al., 2002). However, Great

Lakes sediment records are imperfect recorders of atmospheric lead deposition because of other lead sources such as sewage and run-off, delay between deposition of atmospheric particles into soils and delivery of sediments to lake basins, and mixing effects thereafter. Nevertheless, in lake regions not subject to massive point source influx, gasoline-derived lead was the dominant contributor to the lead inventory in lake sediments after 1930 (Renberg et al., 2002). Although the "new core" temporal trends in lead departed from expectations in the period in which leaded gasoline was phased out (see Methods for possible reasons), both "new core" and Graney et al. (1995) sediment data sets bore significant resemblance to national trends in lead usage in gasoline during the phase-in and peak periods.

Gasoline-derived lead isotopic compositions in North America are thought to reflect temporal changes of lead sources, with a shift towards lower $^{207}Pb/^{206}Pb$ ratios in the 1970s (Shirahata et al., 1980). The suggestion of these trends (1965 to 1980) in both sets of lake sediment data argues that each is a reasonable (although imperfect) proxy of atmospheric lead concentration in the vicinity of Greater Cleveland. The differences in time course and isotope ratios of the two lake core sediments probably arise from differences discussed above with respect to lead concentration. However, at least at one time-point (1982–1984) at which multiple samples of actual atmospheric isotope ratios were available from Akron (a city close to Cleveland), the $^{207}Pb/^{206}Pb$ ratio ranged from 0.816 to 0.833 (Sturges and Barrie, 1987), which encompasses values in both lake sediments at that time period.

4.3. Evaluation of scenarios of Pb exposure and uptake

A perfect proportionality between enamel and lake sediment lead could not be expected because of variation in both data sets (discussed above) as well as possible non-linear relations between lead uptake and atmospheric exposure (Chamberlain, 1983), and the certain contribution of leaded paint to declining but significant baseline levels of tooth enamel lead. Still, the present data are consistent with the hypothesis that from 1936 to 1993, the major lead burden in Cleveland area children rose and fell in concert with atmospheric lead, which was responsible for about two-thirds of total childhood lead uptake in this period. In the descending phase, where trustworthy PbB data are available, the present results are in close accord with previous reports correlating declines in PbB and usage of leaded gasoline (see Introduction). Indeed, excellent correlation was found between reported PbB levels in urban African-American children and lead concentration in enamel formed during the same years. This lends credence to the present findings in tooth enamel and its extrapolation to PbB during the ascending and peak phases, a time when reported data on PbB were either lacking or unreliable (Patterson and Settle, 1976). In addition, multivariate analysis revealed correlation of tooth lead with those neighborhoods that in general had higher 1960–1980 traffic.

Consistent with the results on lead concentrations, $^{207}Pb/^{206}Pb$ ratios in tooth enamel during the peak years of leaded gasoline usage were essentially indistinguishable from those in one set of lake sediments (Graney et al., 1995). Consistency, however, is a necessary but not sufficient proof of relationship because the $^{207}Pb/^{206}Pb$ ratio of other important sources of Cleveland childhood lead uptake, such as paint, is unknown.

The present findings are broadly consistent with those of Farmer et al. (2006) in which lead isotope ratios in dentin-containing teeth in the decades of leaded gasoline usage bore an overall resemblance to those in sphagnum moss (a proxy for atmospheric lead). However, as those authors noted and as mentioned above, the use of tooth dentin rather than core enamel made correlations with contemporaneous atmospheric lead concentration unsuitable.

In sum, all these findings support the thesis that gasoline lead was the predominant lead exposure source of Greater Cleveland children during the years of phase-in, peak, and phase-out of leaded gasoline. The present data, however, do not serve to differentiate between the relative importance of different exposure routes, i.e., direct inhalation of lead aerosols vs. ingestion of gasoline lead-contaminated dust, soil, or food, although EPA estimates indicated that ingestion of leaded dust was a far more important route than inhalation (Tables 1–8 in US EPA, 1986). The same USEPA estimates, although done using atmospheric data obtained after the years of maximum leaded gasoline exposure, illustrate the importance of the summation of lead uptakes from gasoline and non-gasoline sources.

Another factor that probably amplified the combined effects of ingested lead from gasoline and non-gasoline sources is micronutrient (notably Iron) deficiency, which is especially prevalent in low-income communities (Bradman et al., 2001). For instance, multivariate analysis showed that children with high levels of environmental contamination and low ferritin levels had PbB levels about 3 μg/dL higher than those living in less contaminated environments (Bradman et al., 2001). In addition, effects of iron deficiency on lead uptake were larger in younger (1–2 year old) children, i.e. at the time of the 1st and 2nd molar enamel formation, than in much older children (Yip and Dallman, 1984). Wright et al. (2003) also found strong associations between iron deficiency and PbB in 1–4 year old children. The evidence for effects of calcium and zinc deficiencies on lead uptake is somewhat mixed (reviewed in Bradman et al., 2001 and in Schell et al., 2004). In sum, iron and possibly other micronutrient deficiencies may well have played a role in both pre-existing non-gasoline lead uptake in the baseline levels, and in enhancing uptake during the period when leaded gasoline added to the pre-existing and ongoing exposures.

Also, the present results do not cover the first third of the 20th century, when extensive use of leaded paint (Weaver, 1989), or lead in drinking water, food cans, or industrial emissions could have caused an earlier peak in childhood lead exposure.

The data are not consistent with the scenario (see Introduction) in which exposures from other dominant sources were so large just prior to the introduction of leaded gasoline, that lead uptake (and tooth enamel concentration) would continuously decline from 1936 to 1993 as exposure to all such non-atmospheric sources declined. However, during the phase-out of leaded gasoline, the co-incident turnover or renovation of older leaded paint homes, the elimination of soldered food cans (Bolger et al., 1992) and reduction of industrial lead sources could have contributed to the drop in tooth lead.

Lead deposited in soil during the entire period of usage of leaded gasoline years might accumulate and persist in urban soil, remaining an intense source of childhood exposure. This would be especially true of the inner city Cleveland area in which automobile traffic had been considerable during the height of exposure to leaded gasoline. If so, in the extreme, one would expect that tooth lead levels in these urban children would remain at high levels after the phase-out of leaded gasoline, and that tooth isotope ratios would stay similar to those observed in Lake Erie sediment during the peak years. In fact, neither of these outcomes was observed, which is consistent with the observation of a major decline in population PbB levels after the peak years, as reported by others (see Introduction).

The present results, showing close correspondence between atmospheric lead and childhood lead uptakes, do not necessarily conflict with studies showing that soil, especially in heavily trafficked cities, is a persistent source of lead uptake in children (e.g. Mielke et al., 1983; Mielke and Reagan, 1998; Mielke, 1999), especially in "hot spots" of high soil lead along traffic corridors. Rather, other environmental sources of lead exposure (e.g dust and deteriorated paint in older homes, cf. Lanphear, 2003) became predominant sources of childhood lead uptake once the atmospheric contribution had greatly declined. Indeed, lead concentration in enamel did not fall to near-zero after elimination of leaded gasoline, as would be expected if gasoline had been the exclusive source of human lead exposure.

4.4. Public health significance

Since the data on tooth lead concentration were found to be highly and linearly correlated with nationally reported PbB values in urban African-American children, the PbB during the peak years of maximum leaded gasoline usage (1960–1975) could be estimated at about 48 μg/dL. This value is consistent with reported PbB in urban children during near-peak years of leaded gasoline usage (summarized in Lin-Fu, 1972; Billick et al., 1979), despite possible methodologic limitations of those earlier analyses (e.g. Patterson and Settle, 1976; Everson and Patterson, 1980). Also, since in the 1976–1980 national studies (Mahaffey et al., 1982), PbB in white urban children was 75% of that in African-American urban children, an estimated peak PbB of about 36 μg/dl might be expected in the former group.

If there were indeed a peak mean lead level of 48 μg/dl in Cleveland's African-American children, the apportionment estimate indicated that about one-third was due to non-gasoline sources (e.g. leaded paint, food cans) and the remaining two-thirds to leaded gasoline. This elevated "combined" lead level meant that with additional exposure from chewing on leaded paint chips, children would more readily reach toxic levels, as was reported in this period (Lin-Fu, 1972). Indeed, 4 exceptionally high enamel lead levels were found during the years of maximum of childhood lead uptake (Fig. 1).

A PbB level of 48 μg/dl (corresponding to the maximum lead values found in teeth) would be associated with neuropsychological, behavioral and patho-physiological deficits (Lidsky and Schneider, 2003; ATSDR, 2007), and many children undoubtedly had far higher levels than the mean. For instance, in one study, there was a linear relation between childhood PbB and loss of brain volume (the highest PbB reported being about 32 μg/dl, Cecil et al., 2008), and in another study, children with PbB's at age 5 of 25 μg/dl showed a 16-point deficit in IQ (Chen et al., 2005). Again, children with tooth leads that would be equivalent to 35.5 μg/dl PbB had significantly higher difficulty with verbal and auditory processing, attention (reaction time) and dysfunctional classroom behavior (Needleman et al., 1979). Still, in one prospective study of children with PbB levels of 30–40 μg/dl from ages of about 1 through 7, smaller residual changes in IQ and other behavioral measures were found (Wasserman et al., 1997). Nevertheless, in other possibly related prospective studies, Wright et al. (2008) found over 2.5 fold increases in juvenile arrests for violent crimes for children with mean PbB of only 26 μg/dl, and Dietrich et al. (2001) found increases in later delinquent and antisocial behaviors related to high childhood lead levels (their highest values were about 34 μg/dl). Similar conclusions were also reached using environmental data on childhood exposure (Nevin, 2000, 2007). Therefore, it is likely that still greater changes would be expected in contemporary African-American adults, 25–40 years old in 2010, whose teeth showed the equivalent of a PbB of 48 μg/dl at the peak of lead uptake from leaded gasoline. In addition, children born to women whose bone stores of lead were largely formed during the period of peak leaded gasoline exposure, might also be affected due to extensive mobilization of lead from bone during pregnancy and the postpartum period (Gulson et al., 2003). A direct test of these hypotheses with clinical and social data on African-American Cleveland adults of these cohorts would be appropriate aims for further studies.

As of 2009, at least 3 countries still use primarily leaded gasoline, and several use both leaded and unleaded gasoline (UNEP, 2009). The present results, correlating atmospheric lead and childhood lead burden, affirm the need to discontinue use of leaded gasoline in these countries at the earliest moment, even if, as in some countries, other sources of lead exposure are also major (Finkelman, 1996).

Acknowledgments

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