STUDY OF CHILDREN'S BLOOD LEAD LEVEL AFTER PHASE-OUT OF LEADED FUEL USE IN BOMBAY, INDIA

by

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(Under the Direction of Luke Naether)

ABSTRACT

Tetra-Ethyl Lead was added to gasoline worldwide as an ‘anti-knock’ agent in the early 1920s. Although leaded gasoline resulted in widespread environmental contamination, its usage was continued in several countries until the late 1990s. Various studies have associated unleaded gasoline with lower blood lead levels (BLLs) in children. The present study analyzed BLLs in 754 children under the age of 12 years in Bombay, India during 2002-2003, after the phase-out of leaded gasoline. This data was compared with a study done before the phase-out of leaded gasoline, which found that 62% of children aged < 12 years had BLL > 10 µg/dL. We also tested for seasonal variations in pediatric BLLs by comparing data from the nonmonsoon season and the monsoon season. The overall geometric mean BLL of 8.36 µg/dL found in this study was lower than the Centers for Disease Control and Prevention’s level of concern (10 µg/dL). This marks a significant success of the public health system, which was achieved by the removal of lead from gasoline. In the future, emphasis should therefore shift towards other sources of lead exposure.

INDEX WORDS: Pediatric blood lead levels, Particulate Matter, PM10, Air lead levels
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DEDICATION

This work is dedicated to Mary and my family members.
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CHAPTER ONE

FOREWARD

Chapter 1 outlines the information presented in each of the following chapters. Chapter 2 serves as an introduction and background for the present study, describing the history of the use of lead and its phase-out from gasoline in various countries around the world. The pharmacokinetics and clinical manifestations of lead in the human body are also described, as is the screening test of choice for lead exposure-Blood Lead Level (BLL). A range of studies from around the world from before and after the phase-out of leaded gasoline are reviewed. The present study highlights the significant drop in children’s BLL in Bombay, India after the phase-out of leaded gasoline. The present study also studies seasonal variations in BLL and levels of lead in airborne particulate matter samples. Chapter 3 is the manuscript to be submitted in March 2004 to the Journal of Applied Environmental Health Science and Public Health. The manuscript describes the present study under sections such as introduction, methods, results, discussion and conclusions. Chapter 4 presents conclusions and a summary based on the findings of the present study.
CHAPTER TWO

INTRODUCTION

2.1 Introduction

Lead is a heavy metal that is ubiquitous in the environment. It is a naturally occurring component of the earth’s crust. It exists as organic (tetra-ethyl lead, tri-ethyl lead and tetra-methyl lead), inorganic and elemental lead. Lead is soft, malleable and resistant to corrosion. It is a poor conductor of heat and electricity. Due to these properties, lead has been used in a wide variety of applications, such as mining, refining, battery manufacturing, smelting, painting and ceramic glazing (Habal, 2002).

Organic lead (tetra ethyl lead and tetra methyl lead) was added to gasoline as an ‘anti-knock’ agent to achieve desired octane numbers in the early 1920s in the United States (Litvak-Factor, 1999; Schuhmacher, 1996). The combustion of leaded gasoline accounted for 80-90% of airborne lead in large cities in which the leaded gasoline was used (Lovei, 1999). The highest amount of lead in gasoline (0.84 g/L) was used in Cape Town, South Africa (1984) and in Christchurch, New Zealand (1978-1985) (Thomas, 1999). In the United States, the amount of lead in gasoline was 0.465 g/L (1976), 0.394 g/L (1977), 0.349 g/L (1978), 0.306 g/L (1979) and 0.30 g/L (1980) (Thomas, 1999).

The use of leaded gasoline in the United States was banned in 1976 (Habal, 2002). Meanwhile, many developing countries continued to use leaded gasoline. As late as 1999, only 29 out of 192 countries in the world had phased lead out from gasoline (Lovei, 1999).
2.2 Pharmacokinetics of lead

Pharmacokinetics is the process by which a drug is absorbed, distributed, metabolized and eliminated by the body. The primary routes of exposure to lead are inhalation and ingestion. Organic lead is also absorbed to a significant degree through the skin.

Children absorb up to 40% of ingested lead, while adults absorb around 10-15% of ingested lead (Centers for Disease Control and Prevention [CDC] Report, 1991). The gastrointestinal absorption of lead from nonfood sources decreases in the presence of food. Lead in water is absorbed to a greater degree than lead in food. Furthermore, dietary deficiencies in iron and calcium enhance the absorption of lead from the gastrointestinal tract (Goyer, 2001). In blood, 98-99% of lead is present in red blood cells and is bound to hemoglobin (Klaassen, 2001). In children, 75% of the total body lead burden is present in the skeleton (Aro, 2002). The rest is present in soft tissues such as the brain, kidneys and the liver. The liver P450 enzymes in the human body convert tetra ethyl lead (TEL) to tri-methyl lead and inorganic lead. The major route of lead excretion is urine, but lead is also excreted in feces, sweat, hair, nails and breast milk (Goyer, 2001). Plasma lead constitutes 2% of the Blood Lead Level (BLL); it is of more toxicological significance than BLL since it is available for exchange with peripheral tissues such as the nervous tissues (Avila-Hernandez, 1998).

2.3 Clinical manifestations of lead toxicity

The clinical manifestation of lead toxicity is called ‘Plumbism’. Lead toxicity is a cause of concern in children in both developed and developing countries. Children who are three years of age or younger are more likely to be exposed to lead than adults and are more vulnerable to
lead toxicity than adults. One reason children are more vulnerable is because the blood brain barrier, which consists of layer of endothelial cells, is underdeveloped below the age of three years. One reason children are more likely to be exposed is that there is more hand-to-mouth activity in children than in adults (Agency for Toxic Substances and Disease Registry [ATSDR], 1999).

The diagnosis of lead poisoning is based on measuring Aminolevulinic Acid (ALA), Coproporphyrin in urine and Zinc Protoporphyrin (ZPP) in blood (Klaassen, 2001). The screening test of choice is BLL, since ZPP is not elevated in children when BLLs are lower than 25 µg/dL (Klaassen, 2001). BLL is expressed in micrograms per deciliter (µg/dL). Although no threshold has been determined for the harmful effects of lead in children, a 1991 CDC Report has put the BLL of concern in children at 10 µg/dL. This level of concern has been continually reduced over the past few decades, from 60 µg/dL (1960), to 30 µg/dL (1970), to 25 µg/dL (1985), to 10 µg/dL (1991) (CDC, 1991). The main aim of this reduction is primary prevention against the adverse effects of lead. The U.S. Department of Health and Human Services’ Healthy People 2010 initiative has set a national goal of eliminating BLLs ≥10 µg/dL among children aged 1-5 years by the year 2010 (Meyer, 2003).

Effects of lead on cognition in children

Several studies have documented an inverse association between elevated BLLs and cognition in children. In 1979, Needleman et al. measured the dentine lead levels of 2146 children from the primary schools of Chelsea and Somerville in Massachusetts. The performance of 58 children with high dentine lead levels was compared to that of 100 children with low dentine lead levels. Children with elevated tooth lead levels showed poor performance on the Wechsler Intelligence Scale for Children-Revised (WISC-R) IQ test, in language
processing, and on reaction time, a measure of attention. Teachers administered a structured questionnaire to 2,146 children whose teeth were analyzed for lead to evaluate their behavior. Poor classroom behavior was associated with high tooth-lead levels in a dose-dependent manner.

In 1990, Needleman et al. analyzed twelve studies (seven studies on blood lead and five studies on tooth lead) of childhood exposures to lead in relation to cognition. The outcome variable was cognition. From 75 to 724 children were recruited for these studies. The statistical analysis indicated that the partial correlation coefficients between elevated lead levels and cognition were -0.27 to -0.003. This indicated that cognition was lowered with an increase in tooth lead levels and BLLs. Multiple regression analysis suggested that the p-values for association between elevated lead levels and cognition for both blood lead and tooth lead studies were statistically significant (p< 0.05). The authors concluded that lead induced IQ deficits, even at low lead levels.

Lead impairs children’s IQ, beginning at low levels. In a 1996 study of 375 Australian children from 11 to 13 years old, Tong et al. found that the mean scale IQ was reduced by 3.0 points (95% CI of 0.07 to 5.93) for an increase in lifetime average BLL from 10 µg/dL to 20 µg/dL. A 1997 study of 309 seven-year-old Yugoslavian children done by Wasserman et al. showed that a lifetime change in BLLs from 10 µg/dL to 30 µg/dL was associated with a decrease of 4.3 full-scale IQ points, 3.4 verbal IQ points and 4.5 performance IQ points. Language ability is strongly affected by lead. In a 2002 study done by Wang et al. of 934 primary school children aged 8-12 years in Kaohsiung City, Taiwan, it was shown that class rankings in Natural Science, Mathematics, Chinese and History were adversely affected by elevated BLLs. These children had lower class grades in Chinese than in Mathematics. BLLs had a stronger influence on children’s language ability (Chinese) than on their ability to calculate
Reduction in BLL with aging does not necessarily produce an improvement in cognition. The cognitive deficits produced due to exposure to environmental lead during the early childhood years are only partially reversed with a decline in BLLs in the late childhood years (Tong, 1998).

**Effects of lead on the hematopoietic, renal and gastrointestinal systems**

Lead inhibits various enzymes involved in the synthesis of heme (Ferrochelatase and Aminolevulinic Acid Dehydratase [ALA-D]). Lead-induced anemia is hypochromic and microcytic. The enzyme ferrochelatase catalyses the insertion of iron into protoporphyrin rings; failure to insert iron results in the accumulation of protoporphyrin. This combines with zinc to form ZPP, which is intensively fluorescent. The reduced activity of ALA-D results in increased levels of Protoporphyrin IX, Aminolevulinic Acid (ALA) in blood and an increased excretion of ALA in urine. Basophilic stippling is due to the inhibition of the enzyme Pyrimidine-5-Nucleotidase. Basophilic stippling is, however, not a diagnostic feature of lead poisoning. Lead causes a fanconi-like syndrome manifested as glycosuria, phosphaturia and aminoaciduria. The gastrointestinal manifestations of lead poisoning include severe colic pain (lead colic), anorexia, diarrhea and constipation (Klaassen, 2001).

**Effects of lead on the nervous system**

The adverse effects of lead in infants and children involve the nervous system (ATSDR, 1999). Lead stimulates protein kinases and affects the blood brain barrier and neuronal networks within the brain (Goldstein, 1990). Lead disrupts the blood brain barrier by primary injury to the astrocytes and by secondary injury to the endothelial cells. Lead-induced neurological damage occurs in the cerebral cortex, cerebellum and hippocampus (Finkelstein, 1998). Lead-induced encephalopathy is more common in children than in adults. It is manifested as vomiting,
irritability, headache, vertigo, insomnia, clumsiness, loss of appetite, dizziness, ataxia, delirium with tonic-clonic seizures, lethargy, unconsciousness, coma and death. There is cerebral edema, with extravasation of the fluid from the brain capillaries (Klaassen, 2001).

2.4 History of phase-out of leaded gasoline around the world

A partial timeline of the phase-outs of leaded gasoline from various countries around the world is presented in Table 2.1. In 1999, the countries that had completely phased out lead from gasoline were Antigua and Barbuda, Argentina, Austria, The Bahamas, Bermuda, Bolivia, Brazil, Canada, Columbia, Costa Rica, Denmark, The Dominion Republic, El Salvador, Finland, Germany, Guatemala, Haiti, Honduras, Hungary, Japan, Mexico, Nicaragua, Norway, Saba, The Slovak Republic, St. Eustasius, Sweden, Thailand and The United States (Lovei, 1999).

2.5 Previous studies on children’s BLLs

The following is a summary of select studies of children’s BLLs done across the world, before and after the introduction of unleaded gasoline. All these studies clearly highlight a strong relationship between lead in gasoline and BLLs; the BLLs were elevated during the times of leaded gasoline use, and BLLs reduced significantly when gasoline was made lead free. A tabular summary of these studies is shown in Table 2.2

Studies associating leaded gasoline with elevated BLLs

The use of leaded gasoline is a major contributor to elevated BLLs in children. In a 1998 study by Heinze et al., 131 children aged 6-8 years were selected from four public elementary schools (two in the central and two in southern districts) in Jakarta, Indonesia. Measurements of the BLLs, ZPP and hemoglobin levels quantified the exposure assessment for lead.
Environmental samples from tap water and soil were also analyzed for lead. The mean BLL in the central district was $8.3 \pm 2.8 \mu g/dL$; and in the southern district it was $6.9 \pm 3.5 \mu g/dL$. The results of this study showed that 26.7% of the children had BLLs $>10 \mu g/dL$. The proportion of children with ZPP $>70 \mu mol/mol$ was 24%, while 70% of the children were anemic. The lead concentration of tap water did not exceed 0.01mg/L; the lead content of the soil was in the range of 77-223 ppm. The authors concluded that residence in urban areas was a risk factor for the development of elevated BLLs.

High environmental lead concentrations occur in urban areas where leaded gasoline is used. In a 2001 study of 779 primary school children aged 4-12 years in Dhaka, Bangladesh, the geometric mean (GM) BLL was 15 $\mu g/dL$ (4.2-63.1$\mu g/dL$). These schools were selected to include both higher and intermediate socioeconomic class among primary school children from different geographical areas in Dhaka. Of these children, 87.4% had BLLs $>10 \mu g/dL$. The risk factors for the development of elevated BLLs were pica behavior, illiteracy of the parents, residence near major roads and increasing age. Exposure to leaded gasoline was identified as the major contributor to the children’s elevated BLLs. However, the sample size was not representative of the entire pediatric population of Bangladesh, and all sources of lead exposure were not analyzed in the study (Kaiser et al, 2001).

In 2002, a cross-sectional study of 400 children aged 3-5 years was conducted by Rahbar et al. in five diverse communities of Karachi, Pakistan (City Center, Suburbs, Baba Island and Gadap). In the city center, one apartment was selected randomly from every fifth building, and children from this apartment were included in the study. Children from the suburbs and from Baba Island were recruited in a similar manner. In the rural areas (Gadap), four villages were randomly selected, and all houses with at least one child were included in the analysis. The
results indicated that 80% of the children had BLLs $>10 \mu g/dL$; the overall mean was 15.6 µg/dL. Surma (Kohl\(^1\)) application, parental occupational exposure to lead, low parental education, hand-to-mouth activity of the children and residence near main intersections in the city center contributed to children's elevated BLLs. Area-specific factors were not identified, and potential sources of lead exposure other than cooked food, drinking water and dust samples were not analyzed for lead.

In 2002, Rubin et al. evaluated the lead exposure in 1,101 Russian children aged 2-7 years in Ekaterinburg, Krasnouralsk and Volgograd. Kindergartens and preschools were selected in these cities on the basis of their proximity to industrial and traffic sources. The GM BLL of these children was 7.2 µg/dL (2.0-41.7 µg/dL). Of the children, 23% and 1% had BLLs ≥ 10 µg/dL and ≥ 20 µg/dL, respectively. The highest GM BLL was observed in Krasnouralsk (10.7 µg/dL); the proportion of children with elevated BLLs in Krasnouralsk was 60%. Lead was detected in soil samples from Krasnouralsk, and lead levels were elevated in paint samples obtained from Volgograd. This study identified lead contamination of the dust and soil from the use of leaded gasoline and from industrial emissions as major routes of lead exposure. Rural children were excluded from the study, and the schools were not selected randomly.

In 2003, Albalak et al. conducted a study of school children aged 6-12-years in Jakarta, Indonesia to determine the distribution of elevated BLLs. A cluster design was used for this study. Forty primary schools were randomly selected, and a random sample of fifteen second and third grade children in each of these forty schools was selected for inclusion in the study. After adjustment for clustering, the actual sample size was calculated to be 397. The overall GM was 8.6 µg/dL (2.6-24.1 µg/dL). The percentage of children with BLLs ≥ 10 µg/dL and ≥ 20

\(^1\) Kohl is eyeliner that contains 34-90% lead sulfide by dry weight. The color ranges from dark black to gray-brown.
µg/dL was 35 and 2.4, respectively. The percentage of children with BLLs of 10-14.9 µg/dL was 25. Factors such as parental education, parental occupational recycling of metals, home varnishing and water collection techniques were associated with elevated BLLs. The findings were in agreement with the results of similar studies in other countries that used leaded gasoline, but the results of this study could be generalized only to second and third grade children in Jakarta. Lead was not measured in soil, dust and air in the study. The difference in BLLs between the participants and non-participants could not be determined.

**Studies associating unleaded gasoline with lower BLL**

The transition from leaded gasoline to unleaded gasoline has resulted in a fall in children’s BLL. In the United States, National Health and Nutrition Examination Surveys (NHANES) estimate lead exposure. NHANES II and III studies showed that the percentage of children with elevated BLLs (BLLs ≥ 10 µg/dL) in 1-5-year-old children was reduced from 88.2% (1976-1980), to 8.6% (1988-1991), to 4.4% (1991-1994), to 2.2% (1999-2000). In a 2003 review of these data, Meyer et al. suggested that these reductions in the U.S. were due to the removal of lead from gasoline, food and soft drink cans, paints and solder in household plumbing.

In a 1996 study of 252 children aged 6-15 years and 250 adults aged 16-65 years from Tarragona Province, Spain, Schuhmacher et al. evaluated the impact of a reduction in the lead content of gasoline (from 0.4 to 0.15 g/L) on population BLLs and hair lead levels. The BLLs in adults was reduced from 12 µg/dL to 6.3 µg/dL (a 47.5% decrease) and the hair lead levels in children was reduced from 8.8 µg/g to 4.1 µg/g (a 53% decrease). These reductions were attributed to the reduced use of leaded gasoline (Schuhmacher, 1996).
Bitto et al., in a 1997 study, conducted a survey of 1,401 Hungarian preschool children aged 0-4 years old to determine the prevalence of elevated BLLs after the reduction of the lead content of gasoline. Thirteen hospitals were included in the analysis. The mean BLL was 5.7 µg/dL (3.5-6.5 µg/dL), and 4.7% of the children had BLLs > 10 µg/dL. The proportion of children above 15 µg/dL and 20 µg/dL was 1.1% and 0.2%, respectively. The lead content of gasoline was reduced from 0.7 g/L (end of 1984), to 0.4 g/L (1985-1990), to 0.3 g/L (1991), to 0.15 g/L (1992). The mean BLL in these Hungarian children was reduced from 20 µg/dL in the 1980’s, to 6.9 µg/dL in 1994, to 5.7 µg/dL in 1997. The authors stated that the BLLs of children decreased due to a reduction in the lead content of gasoline.

In a 1998 study, Ponka et al. evaluated the concentration of lead in ambient air and in children’s blood in Helsinki, Finland. The concentration of lead in the blood of children aged 1-8 years in a day care center in 1983 (N=29), 1988 (N=17) and 1996 (N=18) was 4.8 µg/dL, 3 µg/dL and 2.6 µg/dL, respectively. The lead content of gasoline was reduced from 0.35 g/L (1983), to 0.14 g/L (1988), to 0 g/L (1996). The authors concluded that a reduction in lead emissions had a beneficial effect on BLLs in children.

In their comprehensive 1999 study, Thomas et al. analyzed the effects of reduction in the lead content of gasoline on population BLLs and on air lead levels, in data obtained from 19 countries. When the lead content of gasoline was reduced to zero, a median BLL of 3 µg/dL and an air lead level of ≤ 0.2 µg/m³ were attained.
2.6 Seasonal variations in BLLs

Seasonal variation in BLLs has been reported in previous studies from developed countries (Yiin, 2000; Aro, 2002). Children exhibit a peak in BLLs during the summer season and a secondary peak during the winter season. The summer peak in BLLs in children is related to an increase in exogenous exposure to lead due to increased playing patterns. The winter peak is related to an increase in the endogenous mobilization of lead from the skeleton due to reduced exposure to sunlight, lower levels of activated vitamin-D3 and enhanced bone resorption (Aro, 2002). In 2000, Yiin et al. studied seasonal changes in residential dust lead content in relationship to BLLs in preschool children. The mean BLL during the hot and cold months was 10.77 µg/dL and 7.66 µg/dL, respectively. The authors attributed the seasonal variation in BLLs to increased exposure to lead in dust and in soil during the summer months.

2.7 Lead toxicity in India

India is the second most populous nation in the world, next only to China. Although India occupies only 2.4% of the world's land area, it supports over 16% of the world's population. In order to better illustrate the socio-economic conditions of people in India, Table 2.3 compares a few key parameters for India against the United States for data in the year 2001 (World Bank Data, 2001). One focus for lead toxicity studies in India has been Bombay, an industrialized metropolitan city in India. In 2001, the population of Bombay was 11.9 million people, with a population density of 20,022 people per square kilometer (Census of India, 2001). In March 1999, there were one million vehicles in Bombay (Tripathi, 2001).
Sources of lead exposure in India

The sources of lead exposure in India include combustion of leaded gasoline, occupational exposure to lead (silver refining, lead battery recycling, printing presses), lead-based paints, lead-glazed ceramics, cosmetics (Kohl) containing lead, herbal medicines (Ayurveda) and the use of cooking vessels such as pressure cookers (Tandon, 1999).

Lead in herbal medicines and Kohl

In the Indian subcontinent, the use of Kohl and Ayurvedic medicines deserves special mention. Kohl is widely used eyeliner that contains 34-90% lead sulfide by dry weight. The color varies from dark black to gray-brown (Vijayalakshmi, 1999). A 2002 study by Rahbar et al. done in Karachi (Pakistan) identified Kohl as an important contributor of children’s elevated BLLs.

Ayurvedic herbal medicines contain lead and mercury as active ingredients. The various medicines under this category include Chyavanprash (7.3 µg of lead/g), Ghasard (16,000 µg of lead/g), Sankhvati (13 µg of lead/g) and Hepatoguard (0.4 µg of lead/g) (Jaffery, 2001). Tait et al. (2002) reported that the ingestion of lead-containing herbal medicines by an Indian woman during pregnancy resulted in elevated maternal BLLs; the newborn had encephalopathy, with the highest BLL recorded for any surviving neonate. Lead-containing herbal medicines were identified as the main source of this neonatal lead poisoning.

Lead-glazed ceramics

Several studies have reported the use of lead glazed ceramics as a contributor to the elevated BLLs in children (Romieu, 1994; Romieu, 1995; Carrillo, 1996). The ceramics are used to store or cook food; lead leaches out from the ceramics into the food during storage or cooking. When tomato juice, fruit juice or cola drinks are stored in lead-glazed ceramics, lead leaches out
of the ceramics and remains in the solution due to the low pH of the stored products. In India, the use of lead-glazed ceramics as a determinant of elevated BLLs in children has not been reported.

**Lead in paints**

After the 1999 George Foundation Study Conference, 24 paint samples were collected from six paint companies in Bangalore and Chennai, India. These paint samples were then analyzed for lead in Adelaide, Australia. Out of 24 samples, 17 samples had lead concentrations > 0.5 % lead by weight; 13 samples had lead concentrations > 1%; and 5 samples had lead concentrations > 10% by weight. Lead pigments present in paints are called lead-chromites. As of 1999, there was limited regulation of the lead content of paints in India, and there were no regulations for labeling the paint cans to indicate lead content (Alphen, 1999).

**Occupational exposure to lead**

In the Indian subcontinent, lead poisoning is not uncommon among the silver refiners. A survey of 50 Indian silver refiners conducted by Tandon et al. in 2001 found that the majority of the silver refiners had clinical features suggestive of lead poisoning (a lead line along the gingival margin, emaciation, low hemoglobin levels and lead colic). There was a reduction in ALA-D, thiamine levels in the blood and increased urinary excretion of ALA in these workers.

**Leaching of lead from Indian pressure cookers**

A vast majority of Indian people use pressure cookers for preparing their food. Lead leaches out from the pressure cookers during the cooking process. The rubber gasket in pressure cookers contains high lead levels; in addition, the safety valve is made of an alloy that contains lead. The rubber gaskets and the safety valves contribute to the contamination of the cooked food (Raghunath, 1998).
**Role of leaded gasoline in children’s BLLs**

Previous studies from all over the world have isolated leaded gasoline as the single most significant source of lead exposure. In order to reduce lead exposure to the general population, the Indian authorities began a phase-out of lead from gasoline in the late 1990s.

In India, the lead content of gasoline during the period of 1986-1996 was in the range of 0.15-0.80 g/L. 70% of the gasoline had lead in the range of 0.15-0.18 g/L and 30% of the gasoline had lead in the range of 0.56-0.80 g/L (Tripathi, 2001; Raghunath, 1999). Low-leaded gasoline (0.15 g/L) was introduced in four metropolitan cities-Bombay, Delhi, Calcutta and Chennai- in June 1994. Unleaded gasoline (0.013 g/L) was introduced in April 1995, on a partial basis, in all four metropolitan cities (Tyagi, 1999). The use of leaded gasoline was banned in February 2000 (Jaffery, 2001).

**Previous studies on lead poisoning in India**

In 1997, the George Foundation (The George Foundation Report, 1997) initiated a major study called ‘Project Lead Free’ on lead poisoning in India. A total of 22,000 people (adults, children and pregnant women) from seven major Indian cities--Bangalore, Calcutta, Bombay, Delhi, Chennai, Hyderabad and Vellore-- were screened. Preschool children, low socioeconomic status school children, pregnant women, soldering unit workers, battery and paint industry workers, traffic policemen and garage workers were included in the study. A total number of 1,852 children (including 291 children from Bombay) were tested. The George Foundation study found that 40% of the children under the age of 12 years in Bangalore, 61.8 % of the children under the age of 12 years in Bombay and 54% of the children under the age of 12 years in India’s capital city, New Delhi, had BLLs > 10 µg/dL, respectively.
Several studies on lead poisoning in Bombay were conducted before the phase-out of lead from gasoline. In a 1997 study, Tripathi et al. determined the dietary intake of heavy metals by the general population of Bombay City. The atmospheric mean concentrations of lead during the period of 1992-1994 were in the range of 0.10-1.12 µg/m³. The total intake of lead through air, water and food (30 µg/day) was far below the recommended standards. In a 1999 study, Raghunath et al. assessed the exposures of Lead (Pb), Copper (Cu) and Zinc (Zn) in children aged 6 to 10 year-old in Bombay. About 410 particulate matter samples were also collected. The air concentrations of lead were in the range of 0.10-1.18 µg/m³. The GM BLLs were in the range of 8.6-14.4 µg/dL. Tripathi et al. (2001) analyzed the concentrations of lead in air and children’s BLLs in different suburbs of Bombay. The GM concentration of lead in air at different locations was in the range of 0.10-1.18 µg/m³. The GM BLL of children aged 6 to 10 years in Bombay was in the range of 8.6-14.4 µg/dL.

These studies did not compare the BLL distribution in high-risk groups, such as children, before and after the phase-out of lead from gasoline to determine the effect of reduction in the lead content of gasoline. The present study compares BLL distribution in children after the phase-out of lead from gasoline to previous studies done during the use of leaded gasoline. Additionally, seasonal variation in BLLs has not been reported from developing countries like India. In the present study, we compared the BLLs during the monsoon season (rainy) and nonmonsoon season (winter) in children from Bombay to demonstrate the seasonal variation in BLLs.
2.8 Main aims of our study

We estimated the prevalence of elevated BLLs from a sample of 754 children aged 0-12 years in Bombay. The main aims of the present study were to compare the BLL distribution in children after the phase-out of lead from gasoline to previous studies done during the use of leaded gasoline. We also studied seasonal variation in PM10 (airborne particulate matter with an aerodynamic diameter of less than or equal to 10 microns), air lead levels and BLL.
REFERENCES


Aro SOA and Hu H. Season modifies the relationship between bone and blood lead levels: the normative aging study. *Archives of Environmental Health* 2002; 57 (5): 466-72.


<table>
<thead>
<tr>
<th>Country</th>
<th>Phase-out</th>
</tr>
</thead>
<tbody>
<tr>
<td>China</td>
<td>• In July 1997, 56% of gasoline was unleaded.</td>
</tr>
<tr>
<td></td>
<td>• Total phase-out by year 2000.</td>
</tr>
<tr>
<td>Egypt</td>
<td>• Unleaded gasoline introduced in 1996.</td>
</tr>
<tr>
<td></td>
<td>• Total phase-out by year 1999.</td>
</tr>
<tr>
<td>Hungary</td>
<td>• Banned the distribution of leaded gasoline in April 1999.</td>
</tr>
<tr>
<td>Kuwait</td>
<td>• Introduced unleaded gasoline in October 1998.</td>
</tr>
<tr>
<td></td>
<td>• Convert to total unleaded gasoline by October 1999.</td>
</tr>
<tr>
<td>Malaysia</td>
<td>• In July 1997, 30% of the gasoline was unleaded.</td>
</tr>
<tr>
<td></td>
<td>• Total phase-out in year 2000.</td>
</tr>
<tr>
<td>Latin America and the</td>
<td>• Lead phased out in several countries in 2000, increasing the number of</td>
</tr>
<tr>
<td>Caribbean</td>
<td>lead free countries to 14.</td>
</tr>
<tr>
<td></td>
<td>• Use of lead in gasoline declined from 27,000 tons in 1990 to 6,000 tons</td>
</tr>
<tr>
<td></td>
<td>in 2000 in the Latin American and the Caribbean.</td>
</tr>
<tr>
<td>Year</td>
<td>Age (Yrs)</td>
</tr>
<tr>
<td>------</td>
<td>-----------</td>
</tr>
<tr>
<td>1998</td>
<td>6-8</td>
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<tr>
<td>2001</td>
<td>4-12</td>
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<tr>
<td>2002</td>
<td>2-7</td>
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<tr>
<td>2002</td>
<td>3-5</td>
</tr>
<tr>
<td>2003</td>
<td>6-12</td>
</tr>
</tbody>
</table>
Table 2-3 Comparisons of key socio-economic parameters between India and the US

<table>
<thead>
<tr>
<th>Comparison Parameter</th>
<th>India</th>
<th>United States</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population in Millions</td>
<td>1,000</td>
<td>285</td>
</tr>
<tr>
<td>Area in Sq. Km</td>
<td>3.3</td>
<td>9.6</td>
</tr>
<tr>
<td>Gross National Income per Capita in US$</td>
<td>460</td>
<td>34,400</td>
</tr>
<tr>
<td>Under age 5 Mortality Rate per 1000 children</td>
<td>93</td>
<td>8</td>
</tr>
</tbody>
</table>
CHAPTER THREE

A STUDY OF CHILDREN'S BLOOD LEAD LEVEL AFTER PHASE-OUT OF LEADED FUEL USE IN BOMBAY, INDIA

\[2\]

**ABSTRACT**-Tetra-Ethyl Lead was added to gasoline worldwide as an ‘anti-knock’ agent in the early 1920s. Although leaded gasoline resulted in widespread environmental contamination, its usage was continued in several countries until the late 1990s. Various studies have associated unleaded gasoline with lower blood lead levels (BLLs) in children. The present study analyzed BLLs in 754 children under the age of 12 years in Bombay, India during 2002-2003, after the phase-out of leaded gasoline. This data was compared with a study done before the phase-out of leaded gasoline, which found that 62% of children aged < 12 years had BLL > 10µg/dL. We also tested for seasonal variations in pediatric BLLs by comparing data from the nonmonsoon season and the monsoon season. The overall geometric mean BLL of 8.36 µg/dL found in this study was lower than the level of concern (10 µg/dL). This marks a significant success of the public health system, which was achieved by the removal of lead from gasoline. In the future, emphasis should therefore shift towards other sources of lead exposure.

INDEX WORDS: Pediatric blood lead levels, Particulate Matter, PM10, Air lead levels
Lead is a heavy metal ubiquitous in the environment. It exists as organic, inorganic and elemental lead. Organic lead (tetra-ethyl lead and tetra-methyl lead) was added to gasoline as an ‘anti-knock’ agent to achieve desired octane numbers in the early 1920s (Litvak-Factor 1999; Schuhmacher 1996). By 1999, the combustion of leaded gasoline accounted for 80-90% of the airborne lead in large cities where it was used (Lovei, 1999). There have been serious efforts in developed countries to reduce environmental lead by reducing the lead content of gasoline. However, the exposure to lead through the combustion of leaded gasoline continued in many developing countries. In 1991, the lead content of gasoline sold in South Africa was 0.836 g/L (Schirnding, 1991). In Jakarta, Indonesia, the phase-out of leaded gasoline did not begin until July 2001 (Alabak, 2003). Leaded gasoline was banned in Beirut, Lebanon only in early 2002 (Nuwayhid, 2003). In Poland, the use of leaded gasoline is expected to be banned by 2005 (Jarosinka, 2003).

The primary routes for exposure to lead are ingestion and inhalation. Dietary deficiencies in iron, calcium, zinc and phosphorus increases the absorption of lead from the gastrointestinal tract (Agency for Toxic Substances Disease Registry [ATSDR], 1999). In vivo, lead mimics and competes with calcium (Needleman, 2004). The most important adverse effects occur in the central nervous system (CNS); the developing CNS is more vulnerable to toxicants than the mature CNS (Needleman, 2004). A higher gastrointestinal absorption rate, frequent hand-to-mouth activity and the sensitivity of their nervous systems make children more vulnerable and more susceptible to lead toxicity than adults (ATSDR, 1999).
Blood Lead Level (BLL) is expressed in micrograms/deciliter (µg/dL). The Centers for Disease Control (CDC, 1991) defines an elevated BLL as ≥10 µg/dL. This level of concern has been continually reduced over the past few decades, from 60 µg/dL (1960-1970), to 30 µg/dL (1970-1985), to 25 µg/dL (1985-1991), to 10 µg/dL (1991) (CDC, 1991).

Lead has no known physiological function in the human body. In children, lead reduces hemoglobin, impairs cognition, retards growth, causes hearing impairment and behavioral problems (ATSDR, 1999). Several studies have shown an inverse association between elevated BLLs in children and cognition (Tong, 1996; Wasserman, 1997; Needleman, 1979; Needleman, 1990 and Canfield, 2003). Canfield et al. (2003) studied 172 children at 6, 12, 18, 24, 36, 48 and 60 months, finding that a higher BLL was inversely associated with children’s cognition at the ages of 3 and 5 years. Other investigators around the world (Tong, 1996; Wassermann, 1997; Needleman, 1979 and Needleman, 1990) have also reported an inverse association between higher BLLs and cognition.

Several studies have been published associating leaded gasoline with high BLLs in children (Heinze, 1998, Kaiser, 2001, Rahbar, 2002, Rubin, 2002 and Albalak, 2003). It was shown that the mean BLL of children was 8.3 ± 2.8 and 6.9 ± 3.5 µg/dL (Heinze, 1998); 7.2 µg/dL (Rubin, 2002); 8.6 µg/dL (Alabak, 2003); 15 µg/dL (Kaiser, 2001) and 15.6 µg/dL (Rahbar, 2002). The percentage of children with BLLs ≥ 10 µg/dL in these studies was 26.7% (Heinze, 1998); 23% (Rubin, 2002); 35% (Albalak, 2003); 87.4% (Kaiser, 2001) and 80% (Rahbar, 2002). The authors suggested that residence in urban areas (Heinze, 1998); pica behavior, illiteracy of the parents, residence near major roads, aging (Kaiser, 2001); Kohl application, parental occupational exposure to lead, low parental education, hand-to-mouth activity, residence near main intersections (Rahbar, 2002); lead contamination of dust and soil
from the use of leaded gasoline and industrial emissions (Rubin, 2002); parental education, parental occupational recycling of metals, home varnishing, and water collection methods (Albalak, 2003) were factors associated with elevated BLLs in children.

A fall in children’s BLLs is related to the phase-out of lead from gasoline. Several studies investigate the association between unleaded gasoline and lower BLLs in children (Schuhmacher, 1996; Bitto, 1997; Ponka, 1998 and Thomas, 1999). In a study done in 1999, Thomas et al. stated that the sources of lead exposure other than leaded gasoline contributed to no more than 3 µg/dL to the overall lead exposure of the general population.

A seasonal variation in BLLs has been reported in previous studies from developed countries (Yiin, 2000; Aro, 2002). Children demonstrate a peak in BLLs during the summer season and a secondary peak during the winter season (Aro, 2002). In 2000, Yiin et al. studied the association between residential dust lead content and BLLs in preschool children in the United States. The authors attributed the seasonal variation in BLL to increased exposure to lead in dust and in soil during the summer months.

In the present study, we monitor BLLs in a pediatric population from the city of Bombay, India. India is the world’s second most populous country; furthermore, Bombay is one of the four major industrialized metropolitan areas in India. In 2001, the population of Bombay was 11.9 million people, with a population density of 20,022 people per square kilometer (Census of India, 2001). In March 1999, there were one million vehicles in Bombay (Tripathi, 2001).

The sources of lead exposure in India include the combustion of leaded gasoline, occupational exposure to lead (silver refining, lead battery recycling and printing presses), lead-based paints, lead-glazed ceramics, cosmetics (Kohl) that contain lead, herbal medicines (Ayurveda) and cooking vessels (pressure cookers) (Tandon, 1999). Low-leaded gasoline (0.15
g/L) became available in four metropolitan cities (Bombay, Delhi, Calcutta and Chennai) in June 1994. Unleaded gasoline (0.013 g/L) was made available in April 1995 on a limited basis in all four metropolitan cities (Tyagi, 1999). The use of leaded gasoline was banned in February 2000 (Jaffery, 2001).

Few papers have been published on lead poisoning in India. The George Foundation in 1997 (The George Foundation Report, 1997) conducted a study of 1,852 children in seven major Indian cities—Bangalore, Calcutta, Bombay, Delhi, Chennai, Hyderabad and Vellore. This study showed that 51.4% of total children had BLLs > 10 µg/dL and 12.6% of the children had BLLs > 20 µg/dL. Analysis of the BLLs of 6-10-year-old children in various suburbs of Bombay indicated that the mean BLL of these children was in the range of 8.6-14.4 µg/dL (Raghunath, 1999; Tripathi, 2001). The concentrations of lead in the air at various locations in Bombay were reported to be in the range of 0.10-1.12 µg/m³ by Tripathi et al. (1997); 0.10-1.18 µg/m³ by Raghunath et al. (1999) and 0.10-1.18 µg/m³ by Tripathi et al. (2001). The seasonal variation in BLLs has not been studied in India.

In the current study, we report the impact of the reduction in the lead content of gasoline on children’s BLLs, the relationship between season and BLLs, and the relationship between season and air lead levels.

3.2 Methods

The study was done in three phases, from July 2002 to August 2003. In phase one (July 2002), we visited the potential sampling locations to lay a foundation for an investigation of pediatric lead exposure in Bombay. The primary objective of this visit was to meet with potential study collaborators in Panchsheel Hospital and view the potential study areas. Our
collaborators from Panchsheel approved the research study proposal and agreed to assist our study.

In India, the seasonal weather patterns are as follows: the rainy season (June through September), the winter season (October through January) and the summer season (March through May). In phase two of the study (December 2002 to January 2003), we performed the nonmonsoon season (winter season) component of our study in Bombay. In Phase three of the study (June through August 2003), we performed the monsoon (rainy season) component of our study.

**Study location**

The study was conducted in Bombay, India (Figure 3.1 and Figure 3.2). The study locations were Panchsheel Hospital (Mulund) and low socioeconomic areas in Mulund and Thane. These locations were selected with the objective of getting a data set that contained a mix of children from different socioeconomic backgrounds. Panchsheel Hospital is a pediatric hospital where children aged 0-15 years are treated for routine pediatric illnesses. Panchsheel Hospital was selected to include children from the middle socioeconomic status (SES) in our study population. The low socioeconomic areas in Mulund & Thane were selected to include children of a lower SES in our study population.

**Study population**

A total of 754 children were included in the study, 276 in phase two (135 from Panchsheel and 141 from low socioeconomic areas) and 478 in phase 3 (184 from Panchsheel and 294 from low socioeconomic areas) (Table 3.1). Parental occupation and geographical location determined the SES. Although our target age group was aged 1-6 years, all children under age 12 years served by Panchsheel or living in the low socioeconomic areas were eligible
for our study. The cutoff point of 12 years was derived from earlier studies on lead poisoning
done in Bombay by the George Foundation. All children- irrespective of their sex, religion,
etnicity and SES were included in the study. Despite intensive efforts to contact them, 205
children (70.4%) of the 276 children from phase two could not be included in phase three of the
study. The remaining 71 children from Phase two were included in phase three.

**Ethical issues in our study**

The research proposal for this study, including English and Hindi translations of the
questionnaire and consent form, was submitted to and approved by the Institutional Review
Board and the Human Subject Research Committee at the University of Georgia.

**Subject recruitment**

Parents of all inpatient/outpatient children at Panchsheel Hospital had the study explained
to them, including the sampling procedures and the significance of the study, and they were
encouraged to have their child or children participate in the study. Parents of children in the low
socioeconomic areas were approached in a similar manner. Parents who voluntarily agreed to
have their child/children participate in this study had a consent form and a questionnaire
administered to them by a trained physician. The questionnaire elicited the following
information: name of the child, sex of the child, residential address, parental occupation history,
birthplace of the child, number of members in the family, medical history of the child and the
nutritional history of the child. The response rate for lower SES children was higher than the
response rate of middle SES children; therefore, there were inconsistencies in the sample sizes of
middle and lower SES children during the phase two and phase three of the study.
Blood collection method

Blood collection and analysis was done according to the protocol provided by ESA Lead Care (ESA Laboratories, Chelmsford, U.S.A). A trained physician collected the blood samples using sterile procedures (sterilized needles, gloves and gauze pieces) to prevent lead contamination of collected blood samples and to prevent transmission of infection. For each subject, the middle finger or ring finger was washed thoroughly with soapy water, cleansed with an alcohol swab, and punctured with a sterilized single-use needle. The first few drops of blood were discarded, and 50 µL of blood was collected in a capillary tube. The exterior surface of the capillary tube was wiped off with sterilized gauze. The blood sample was discarded if air bubbles or blood clots were present in the capillary tube. The blood sample was transferred to a lead-free treatment reagent tube that contained an anticoagulant (Ethylene Diamine Tetra acetic Acid). The anticoagulant was mixed with the blood, and this mixture was kept undisturbed for one minute. About 50 µL of this mixture was transferred to the Lead Care Portable Analyzer (ESA Laboratories, Chelmsford, U.S.A.) by using a 50 µL pipette. The lead care instrument gave the BLL reading in 3 minutes. The minimum BLL detection limit for the instrument was 1.4 µg/dL, and the maximum detection limit was 65 µg/dL. The samples were tested within 48 hours when stored at room temperature and within 7 days when refrigerated. All BLLs analyses were done at Panchsheel Hospital.

As a quality assurance measure, the lead care instrument was re-calibrated after the testing of every 48 pediatric blood samples with a calibration button provided in every new testing kit (each kit contains 48 treatment reagent tubes). Controls vials (standard bovine blood
lead solutions) were tested after the testing of every 100 pediatric patients; the obtained results were within the specified range.

Dr. Vikram Nichani (VN), who carried out the fieldwork for this study, revealed the results of the blood analysis to the parents. The results of the children tested at Panchsheel Hospital were available to their parents in 10 minutes. The results of the children tested in slum areas were available to their parents in 7 days. The BLL reading was explained in relation to the CDC cutoff limit of 10 µg/dL. Since medical evaluation/medical management of the cases with elevated BLLs (≥ 10 µg/dL) was an important component of this study, all cases with BLLs equal to or more than the CDC action limit (10 µg/dL) were referred to a practicing pediatrician at Panchsheel Hospital for follow-up.

**Air sampling**

In addition to BLL measurements in children from Bombay, this study also monitored PM10 levels at Panchsheel Hospital. PM10 is defined as particulate matter of an aerodynamic diameter equal to or less than 10 microns. The PM10 sampling was done during the monsoon (rainy) and nonmonsoon seasons (summer) by colleagues from Sardar Patel College of Engineering (Andheri, Bombay). The PM10 samples were also analyzed for lead content at the same laboratory. The air sampling was carried out with a PM10 high volume sampler at a flow rate of 1.3 m³/min for sample duration of 24-hrs. Lead content was measured by digesting part of the filter paper (40 cm²) and analyzing it for lead by an Atomic Absorption Spectrophotometer. PM10 sampling during March-April of 2003 (nonmonsoon season) corresponded with phase two of this study. In this time period, ten samples were collected at Panchsheel Hospital on ten random days. Out of these, five samples were analyzed for lead content. During the period of September 2003 (monsoon season), which corresponded with
phase three of this study, ten more samples were collected at the same location; out of these, five samples were analyzed for lead content.

3.3 Data analysis

The dependent variable used in the analysis was BLL. The independent variables used in this analysis were age, sex, socioeconomic status (SES) and season. Sex, SES and season were treated as discrete variables, while age and BLL were treated as continuous variables. BLL was expressed as geometric mean (GM) ± geometric standard deviation (GSD). The distribution of BLL was not normal, so we used the Box-Cox transformation to prepare the data for statistical analysis.

The covariates of interest were age, sex, SES and season. We used a multiple linear regression analysis to study the effect of various independent variables on BLLs, with adjustments for confounders at the same time. We used an independent sample ‘t’ test to determine the relationship between categories of discrete variables. A paired sample ‘t’ test was performed on a small subset of the population (71 children) whose blood measurements were repeated in the nonmonsoon (winter) and monsoon seasons (rainy), respectively. A ‘p’ value of 0.05 was considered to be statistically significant.

3.4 Results

The demographics of the study population were as follows. The mean age of the population was 57 months (range 0-143 months). Of the children, 53.3 % were boys, and the remaining 46.7% were girls; 42.3% of the total population was from the middle SES, and 57.7%
was from a lower SES. Out of the total population, 36.6% of the children were sampled in the nonmonsoon season, and 63.4% of the children were sampled in the monsoon season.

The number and percentage of children with BLLs 0-9.9, 10-19.9, 20-29.9, 30-39.9 and ≥ 40 were 504 (66.8%); 222 (29.4%); 21 (2.8%); 5 (0.6%) and 2 (0.2), respectively (figure 3.3). The majority of the children (66.8 %) had BLLs lower than the CDC action limit level of 10 µg/dL. Twenty-seven children required medical evaluation (BLL 20-44 µg/dL), and only one child required medical treatment of lead poisoning (BLL > 65 µg/dL).

The GM BLL and GSD for lower SES and middle SES children were 9.2 (5.8) and 7.3 (3.8), respectively. The GM BLL and GSD for males and females were 9.1 (5.2) and 9.7 (5.3), respectively. The GM BLL and GSD for nonmonsoon season and monsoon season were 7.3 (4.0) and 9.1 (5.7), respectively. The independent sample ‘t’ for SES was a predictor of elevated BLLs (t = -5.9; p=0.000). The independent sample ‘t’ for sex suggested that the association between BLLs and sex was not statistically significant (t =-1.5, p=0.138). However, the independent sample ‘t’ for season suggested that the association between BLLs and season was statistically significant (t =5.2; p=0.000). A tabular summary of BLLs by subject characteristics is given in Table 3.2.

The multiple regression analysis suggested that age, SES, and Season were associated with elevated BLLs (Table 3.5).

3.5 Discussion

Lead poisoning remains a cause of concern in many of third world countries. Environmental pollution is a major hazard in cities like Bombay; this is worsened by the ever-increasing number of automobiles. Lead poisoning is a persistent health problem in India,
especially for children, since exposures to even very small amounts of lead can cause the malfunctioning of almost all the physiological systems of the body. The exposure assessment for lead can be done by measuring the amount of lead in blood or in shed deciduous teeth in children. We used BLLs to study lead exposures, since this is the method of choice for determining lead exposure (CDC, 1997). This discussion will focus on the role of a few sources of lead on children’s BLLs and also the distribution of children’s BLLs with respect to four factors, namely: age, sex, SES and season.

Numerous studies have associated unleaded gasoline with a drop in children’s BLLs. A 1998 study by Pirkle et al. studied the decrease in BLLs of 1-5-year-old children as recorded by the National Health Nutrition Examination Survey (NHANES III) in the United States. The mean BLL was reduced from 3.6 µg/dL in Phase-1 (1988-1991) to 2.7 µg/dL in Phase-2 (1991-1994). The proportion of children with elevated BLLs during this time reduced from 8.6% to 4.4%. The authors suggested that the reduction in mean BLL was due to the removal of 99.8% of the lead from gasoline and the removal of lead from soldered cans. In Athens, Greece, the BLLs were reduced from 16 µg/dL (1982) to 8 µg/dL (1988) when gasoline lead concentrations were reduced from 0.4 g/L to 0.15 g/L (Thomas, 1999). These studies support the hypothesis that lead content of gasoline is a major contributor to the children’s elevated BLLs.

Our study results are consistent with these studies. We recorded a dramatic decrease in children’s BLL in Bombay after the phase-out of lead from gasoline in February 2000. The percentage of children with BLLs > 10 µg/dL was reduced from 62% in 1997 (The George Foundation Study, 1997) during the period of use of lowleaded and unleaded gasoline to 33% in 2003 after the phase-out of leaded gasoline (see Table 3.4). The reduction in the lead burden, as determined by the BLLs, was presumably due to a reduction in the lead content of gasoline. The
overall GM of 8.36 µg/dL is lower than the GM BLL reported in earlier studies from Bombay which were conducted before the phase-out of lead from gasoline. The GM BLL of 7.29 µg/dL recorded during the nonmonsoon season (winter) was also one of the lowest mean BLLs reported in the literature on studies of lead poisoning in Bombay.

Previous studies done in Bombay have shown a positive correlation between air lead levels and children’s BLLs. Tripathi et al. (2001) discovered a positive correlation between BLLs and air lead levels. BLLs in 6-10-year-old children increased by 3.56 µg/dL when air lead levels increased by 1µg/m³. Similar results were obtained by Raghunath et al. (1999). We did not perform linear regression analysis between air lead levels and BLLs due to a limited number of air lead data samples (N=5 for the monsoon season and N=5 for the nonmonsoon season). The recommended ambient air quality standards for lead are 1.5 µg/m³ for industrial areas and 1 µg/m³ for residential areas (Jaffery, 2001). The concentrations of air lead levels in both the phases did not exceed 1µg/m³. We recorded a dramatic fall in air lead levels after the phase-out of lead from gasoline, as compared to those found in previous studies (Tripathi, 2001; Raghunath, 1999). This is likely attributed to a reduction in the lead content of gasoline.

**BLL distribution in relation to age**

Age is one of the risk factors for the development of elevated BLLs in children. Previous studies on lead poisoning have been done on children less than 12 years: 3-5 years by Rahbar et al.; 4-12 years by Kaiser et al.; 6-8 years by Heinze et al.; 6-10 years by Tripathi et al. and Raghunath et al. and 6-12 years by Albalak et al. However, not all studies have shown age as a risk factor for the development of elevated BLLs. A study by Kaiser et al. (2001) showed that the BLLs in 4-12-year-old children in Dhaka, Bangladesh had a positive linear relation with age. BLLs increased with aging in these children. Another study (Romieu, 1995) reported higher
BLLs in older than in younger Mexican children. There was a significant increasing trend in
BLLs with age in children from the residential areas of Tlalpan and the industrial areas of
Xaloston (p=0.0035). Lee et al. (2002) studied the prevalence of elevated BLLs in 918 Korean
children and found that the GM BLL in 8-year-old children was lower than the GM BLL in 11-
year-old children (P< 0.002). Some studies (Schutz, 1997; Kirt, 1997) have reported a negative
relationship between age and BLL. In the United States, Pirkle et al. (1998) analyzed the BLLs
of children < 12 years. The GM BLL for children aged 1-3 years, 3-5 years and 6-11 years was
shown to be 3.1 µg/dL, 2.5 µg/dL and 1.9 µg/dL, respectively. Jacob et al. (2000) showed that
BLLs were higher in young German children as compared to BLLs in older German children.
Rahman et al. (2002) stated that age was not associated with dentine lead levels in children in
Karachi, Pakistan.

Due to pronounced hand-to-mouth activity and a higher gastrointestinal absorption rate,
the BLLs of young children is expected to be higher than that of older children. In addition, the
gastrointestinal absorption for lead decreases with increasing age. Our results of the increase in
BLLs in children with advancing age are consistent with the results of other investigators in
developing countries (Kaiser, 2002; Romieu, 1995; Lee, 2002). The increase in BLL with
advancing age may be related to increased frequency of playing patterns in older children
(Kaiser, 2002). An alternative explanation of the increase in BLL with aging is that rapid growth
in the late childhood years results in an increased mobilization of lead from the skeleton. An
increase in BLL with aging has not been reported in previous studies on lead poisoning in
Bombay. The association between age and BLLs was statistically significant (F=6.1, p=0.0137),
controlling for other confounders at the same time.
BLL distribution in relation to sex

Several studies (Gao, 2001; Wilhelm, 2002; Jarosinska, 2003) have demonstrated a higher mean BLL in males than in females. This may be related to increased environmental lead exposure in boys due to their playing patterns (Gao, 2001). Schuhmacher et al. (1996) discovered that hair lead concentrations in boys were 44% higher than the hair lead concentrations in girls, although the difference was not statistically significant.

Others studies (Heinze, 1998; Rahman, 2002) have proved no difference between mean BLL in males and mean BLL in females. A consistent finding during the phase two and phase three of our study was that the mean BLL of females was 6% higher than that of males. There was no statistically significant difference between the mean BLL of males and the mean BLL of females. In multiple regression analysis, sex was not a significant predictor of elevated BLLs (F=1.2, p= 0.276).

BLL distribution in relation to SES

Pirkle et al. (1998) showed that children from lower income families were at risk of elevated BLLs. Nuwayhid et al. (2003) reported that children from the lower SES and lower educated families had BLLs ≥10 µg/dL than other children who had BLLs < 10 µg/dL (p < 0.01). Jacob et al. (2000) revealed that lower SES was associated with elevated BLLs in children aged 5-14 years.

The GM BLL in lower SES children was 34% higher than the GM BLL of middle SES children in the monsoon season. For nonmonsoon season, the GM BLL for lower SES was 7% higher than the GM BLL of middle SES children. There was a statistically significant difference between the mean BLLs of middle SES and lower SES children. In multiple regression analysis, SES was a significant predictor of elevated BLLs (F=34.2; p=< 0.0001). A higher BLL in lower
SES children as compared to middle SES children is attributed to improved hygienic practices and better nutrition in middle class SES children than in lower SES children.

**BLL distribution in relation to Season**

Seasonal fluctuations occur in BLLs in children, adults and pregnant women. Aro et al. (2002) proved that BLLs in middle-aged and elderly men were higher in winter months than in summer months. Elevated BLLs during winter months were attributed to the mobilization of the bone lead stores due to reduced sun exposure and reduced levels of activated vitamin-D.

Jarosinka et al. (2003) demonstrated the mean BLL in Silesian children to be 10% higher in the spring/summer quarter (non-heating months) than their mean BLL in fall/spring quarter (heating months). The air lead concentrations were lower in non-heating months and higher in heating months. Another study by Nuwayhid et al. (2003) reported a seasonal effect on BLLs in children. Most of the children with elevated BLLs were identified in the summer and fall seasons. Leroyer et al. (2000) showed that BLLs in children aged 8-11 years were higher in summer season than in the winter season.

Our research study differs from previous studies in that the effect of the monsoon season on BLLs was determined. Our results were indicative of a seasonal fluctuation in BLL. The mean BLL in a small subset of the population (71 children) tested in the monsoon season (11.7 \( \mu g/dL \)) was higher than their mean BLL in the nonmonsoon season (9.1 \( \mu g/dL \)). The paired sample ‘t’ test for these children was statistically significant (\( t = -5.1, p=0.000 \)), indicating that the mean BLL of these children in the monsoon season was significantly different from their mean BLL in the nonmonsoon season. There was a statistically significant difference between BLLs and season. In multiple regression analysis, season was a significant predictor of elevated BLLs (\( F=29.0; p =< 0.0001 \)).
Previous studies on lead poisoning in Bombay have found ingestion and inhalation as major routes of exposure to lead for children. Our air lead data supports the contention that there is seasonal variation in both PM10 and air lead levels (see Table 3.3). The mean air PM10 concentration during the monsoon season was lower than the mean concentration during the nonmonsoon season by 80%. The mean air lead concentration in the monsoon season was lower than the mean concentration in the nonmonsoon season by 92%. Mean air lead concentration was lower than the mean air PM10 concentration during the monsoon due to fact that the air lead particles were smaller in size than PM10 particles. The effect of the monsoon season is more pronounced for air lead particles than for PM10 particles. Similar results have been reported in the literature (Larssen, 1994; Kulkarni, 1998).

Since inhalation exposure depends on the concentration of lead in the air and on the total volume of air inhaled, a higher BLL in the monsoon season, in the presence of lower air lead levels, was indicative of ingestion as a major pathway contributing to elevated BLLs in these children during the monsoon season. Ingestion of lead-contaminated soil and/or drinking tap water was a major contributor to elevated BLLs during the monsoon season.

The results support the hypothesis that the monsoon peak in BLLs is at least, in part, due to exposure to environmental lead through the ingestion pathway. It is not prudent to conclude that reduced sun exposure and reduced vitamin-D levels may have caused the mobilization of lead from the skeleton stores during the monsoon season. This conclusion would be based on the assumption that the duration of sun exposure is lower during the monsoon season as compared to the nonmonsoon season. The factors that would mobilize lead from the bone during the monsoon season are also poorly understood. Since the bone lead levels were not measured
during either season, we could not comment on the possibility of mobilization of lead stores from the skeleton during the monsoon season.

3.6 Conclusions and Acknowledgments

We concluded that there is a decreasing trend in BLLs after the phase-out of leaded gasoline (see Table 3.6). We also noted that the monsoon season exerts its influence on BLLs, PM10 levels and air lead levels. Age, SES and season are significant predictors of elevated BLLs. Future studies on other sources of lead exposure are highly warranted for public health purposes. Also, a national population-based study is required to determine the prevalence of elevated BLLs after the phase-out of lead from gasoline.

The present study has a few limitations; one of them is representativeness. The selected population was representative of only Bombay’s urban pediatric population aged < 12 years. A subset (approximately 10%) of the study population was employed to demonstrate a seasonal variation in BLLs during the monsoon and nonmonsoon seasons. Due to limited resources, only a small number of air samples could be analyzed for PM10 and lead. Further, other sources of lead exposure, such as lead in paints, tap water, soil and herbal medicines could not be analyzed.

We are grateful to Dr. Mohan Kodavor, the head of Panchsheel Hospital, Bombay for his support and cooperation in the study. We are also thankful to Dr. Anand Vidyashankar of the University of Georgia for helping us with the statistical analysis of the data. We thank Dr. Milind Kulkarni of Sardar Patel College of Engineering, Bombay for the collection and analysis of the particulate matter samples. Lastly, we are grateful to all the children and their parents who participated in this study.
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Lead care blood testing system.


Needleman HL. Lead poisoning.


Figure 3-1 Map of India
Figure 3-2 Map of Bombay
Figure 3-3 BLL distribution results from present study
Table 3-1 Description of subject population

<table>
<thead>
<tr>
<th>Subject characteristic</th>
<th>Sample size (N)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Location and Socioeconomic status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Panchsheel (Middle SES)</td>
<td>319</td>
<td>42.3</td>
</tr>
<tr>
<td>• Slum areas (Lower SES)</td>
<td>435</td>
<td>57.7</td>
</tr>
<tr>
<td><strong>Age (months)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• 0-23</td>
<td>108</td>
<td>14.3</td>
</tr>
<tr>
<td>• 24-47</td>
<td>191</td>
<td>25.3</td>
</tr>
<tr>
<td>• 48-71</td>
<td>187</td>
<td>24.8</td>
</tr>
<tr>
<td>• 72-95</td>
<td>158</td>
<td>21.0</td>
</tr>
<tr>
<td>• 96-119</td>
<td>104</td>
<td>13.8</td>
</tr>
<tr>
<td>• 120-143</td>
<td>6</td>
<td>0.8</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Male</td>
<td>402</td>
<td>53.3</td>
</tr>
<tr>
<td>• Female</td>
<td>352</td>
<td>46.7</td>
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<tr>
<td><strong>Season sampled</strong></td>
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<td></td>
</tr>
<tr>
<td>• Nonmonsoon</td>
<td>276</td>
<td>36.6</td>
</tr>
<tr>
<td>• Monsoon</td>
<td>478</td>
<td>63.4</td>
</tr>
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</table>
Table 3-2 BLLs by subject characteristics

<table>
<thead>
<tr>
<th>Subject Characteristics</th>
<th>Geometric Mean</th>
<th>Min.</th>
<th>Max.</th>
<th>Std. Dev.</th>
<th>t-test (p-value)</th>
<th>F (p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location &amp; Socio-economic status (SES)</td>
<td>-5.9 (0.0001*)</td>
<td>34.2 (0.0001*)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Panchsheel (Middle SES)</td>
<td>7.3</td>
<td>2.1</td>
<td>31.8</td>
<td>3.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Slums (Lower SES)</td>
<td>9.2</td>
<td>2.8</td>
<td>65</td>
<td>5.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (months)</td>
<td>2.5 (0.0137*)</td>
<td>6.1 (0.0137*)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-23</td>
<td>7.2</td>
<td>2.1</td>
<td>31.8</td>
<td>4.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>24-47</td>
<td>8.1</td>
<td>2.2</td>
<td>65</td>
<td>6.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>48-71</td>
<td>8.3</td>
<td>2.5</td>
<td>31.2</td>
<td>4.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>72-95</td>
<td>8.7</td>
<td>3.2</td>
<td>29.7</td>
<td>4.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>96-119</td>
<td>9.9</td>
<td>3.7</td>
<td>37.4</td>
<td>5.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>120-143</td>
<td>8.3</td>
<td>5.3</td>
<td>12.8</td>
<td>3.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>1.1 (0.28)</td>
<td>1.2 (0.28)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>9.1</td>
<td>2.1</td>
<td>65</td>
<td>5.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Females</td>
<td>9.7</td>
<td>2.2</td>
<td>37.4</td>
<td>5.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Season</td>
<td>5.4 (0.0001*)</td>
<td>29.1 (0.0001*)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonmonsoon</td>
<td>7.3</td>
<td>2.1</td>
<td>31.8</td>
<td>4.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monsoon</td>
<td>9.1</td>
<td>3.2</td>
<td>65</td>
<td>5.7</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Table 3-3 Levels of PM 10 (µg/m³) and lead in air (µg/m³)

<table>
<thead>
<tr>
<th></th>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>PM10</td>
<td>Nonmonsoon</td>
<td>124.1-418.4</td>
<td>273.02</td>
<td>30.84</td>
</tr>
<tr>
<td>Lead</td>
<td>Nonmonsoon</td>
<td>0.18-0.80</td>
<td>0.38</td>
<td>0.10</td>
</tr>
<tr>
<td>PM10</td>
<td>Monsoon</td>
<td>12.7-115.0</td>
<td>56.20</td>
<td>9.54</td>
</tr>
<tr>
<td>Lead</td>
<td>Monsoon</td>
<td>0.03-0.05</td>
<td>0.04</td>
<td>0.000667</td>
</tr>
</tbody>
</table>

### Table 3-4 Comparison of BLLs distribution before and after leaded gasoline in Bombay

<table>
<thead>
<tr>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 10</td>
<td>61.8%</td>
<td>33.2%</td>
</tr>
<tr>
<td>≥ 20</td>
<td>14.7%</td>
<td>3.8%</td>
</tr>
<tr>
<td>≥ 30</td>
<td>2.7%</td>
<td>1.0%</td>
</tr>
<tr>
<td>≥ 40</td>
<td>0.6%</td>
<td>0.3%</td>
</tr>
</tbody>
</table>

### Table 3-5 Interpretation of the multiple regression analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Age</th>
<th>Sex</th>
<th>SES</th>
<th>Season</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interpretation</td>
<td>Every increase in age by one month increases the BLL by 0.0113 µg/dL</td>
<td>The mean BLL of females is higher than the BLL of males by 0.0123 µg/dL</td>
<td>The mean BLL of lower SES is higher than the mean BLL of middle SES by 0.7266 µg/dL</td>
<td>The mean BLL of monsoon season is higher than the mean BLL of nonmonsoon season by 0.5574 µg/dL</td>
</tr>
</tbody>
</table>
CHAPTER FOUR

CONCLUSIONS

4.1 Summary

In recent years, there has been a significant reduction in children’s blood lead levels (BLLs) in India. Although we cannot conclusively prove that the combustion of leaded gasoline was a major contributor of high BLLs in children, our results do support the hypothesis that the use of unleaded gasoline has contributed to a reduction in population BLLs.

We observed a 29% decline in the percentage of children with BLLs > 10 µg/dL between 1997 and 2003 in Bombay, India. During 2002-2003, the overall Geometric Mean (GM) BLL of 8.36 µg/dL was lower than 10 µg/dL. Of the tested children, 33% were found to be BLLs > 10 µg/dL and were consequently at risk of neurobehavioral, IQ deficits and reduced academic achievements. We found that age and socioeconomic status (SES) were associated with elevated BLLs and that there was a seasonal periodicity of BLLs, with blood lead being 24% higher in the monsoon season (rainy) over the nonmonsoon season (winter). The concentration of lead in air in Bombay during the phase two and phase three of our study (Phase 2 and Phase 3) was below the recommended standards.

The high BLLs found in the present study can be attributed to sources of lead exposure other than combustion of leaded gasoline. It is possible that lead in soil, lead in drinking water, Kohl application, ingestion of Ayurvedic herbal medicines, a parental history of exposure to lead
in the workplace and the lead content of lead-glazed ceramics might have contributed to the children’s elevated BLLs. However, study of any of these factors was outside the scope of the present study. The population’s BLLs have reduced after the phase-out of lead from gasoline, but there is a large body of evidence that lead exposure remains a major public health concern in Bombay, especially for lower SES children.

The population of Bombay is mostly unaware of the adverse effects of lead. There has to be an increased public awareness about lead poisoning and the sources of lead exposure through the media. Increased health consciousness is an essential step in reducing children’s BLLs. Lower SES families should be educated to adopt improved hygienic practices. Proper nutritional support of the children is also an important factor in prevention of lead poisoning. In addition, pediatricians should screen those children who are at risk of developing elevated BLLs. Both, primary and secondary preventive strategies are important steps in the eradication of lead poisoning from developing countries.

In our study, only one child out of 754 children was diagnosed with lead poisoning (BLL > 65 µg/dL). This can be regarded as a major success of the public health system, achieved by the removal of lead from gasoline. Nevertheless, it should be noted that the phase-out of lead from gasoline is only a first step in reducing children’s BLLs.
4.2 Limitations of the study

Children were recruited from only two suburbs of Bombay. Therefore, the sample size was not representative of the entire Indian pediatric population. Since the inclusion of children was entirely dependent on parental consent, all patients attending Panchsheel Hospital could not be included in the study. For the same reason, random sampling (picking one child out of say every five) was not possible for the estimation of BLLs. Further, higher SES children could not be included in the study. This study limits itself to lower SES and middle SES due to the study locations in slum areas and a nursing hospital with a primarily middle-class clientele. This being a voluntary participation study, out of the total of 754 children in the pooled data set, only 71 children (approx. 10%) could be repeated in both seasons. This sub-set of 71 children was employed to demonstrate the seasonal variation in BLLs.

The numbers of samples of air particulate matter (PM-10) were too small (N=5 for lead and N=10 for PM-10) to demonstrate a seasonal variation in air lead and PM10 levels. Variables such as a parental history of smoking, pica\(^3\) behavior, parental educational status, parental occupational exposure to lead at the workplace, Kohl application, ingestion of herbal medicines and ingestion of canned foods were not included in our questionnaire and hence in the regression models. Other sources of lead exposure such as the lead content of soil, tap water and paints were not analyzed in the study.

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\(^3\) Pica is a eating disorder in children where they pick at nonfood items and put them in their mouths, like eating mud, pencils, etc.
4.3 Scope of future research

Further studies with larger sample sizes are required to confirm our findings of seasonal variation in BLLs, air lead and air particulate matter levels. A population-based study on a national basis is highly warranted to determine the prevalence of elevated BLLs after the phase-out of lead from gasoline. Further research into other sources of lead exposure for the pediatric population is very important. The contribution of each source to children's blood lead level should be determined and controlled to further reduce the population BLLs to levels lower than the current level of 8.36 µg/dL. Other risk groups, such as pregnant women should be studied to determine the prevalence of elevated BLLs after the phase-out of lead from gasoline.