1. INTRODUCTION

In the present-day situation, the most common and widespread environmental health problem facing mankind, especially young children is lead poisoning. Millions of Indian children have been exposed to lead and now suffer from elevated levels of lead in their bodies.

Once in the body lead can cause a wide variety of physical and mental problems. The problems associated with lead poisoning are compounded by the fact that many people do not know what it is or how their children get it, as users seldom are aware of its presence. It can very well be said that lead is one of the most commonly used, but least seen metals in use today.

1.1. RATIONALE:

Lead exposure poses a major environmental health problem in India. Lead is a potent poison and is harmful in even very small amounts. Once absorbed into the body, lead combines with and inhibits the functioning of certain enzymes – often with severe physiological or neurological consequences.

The global burden of disease estimates that lead accounts for 0.9% of the total disease burden. No direct studies have yet been performed in India to investigate the impact of lead exposure on neurobehavioral development of children. The greatest improvements in estimating the disease burden of lead will come from characterizing the exposure-response relationships for health effects. For the most part, formal dose-response data do not exist and many of the most serious health effects are based on case reports.

At present, it is necessary to make assumptions about the number of people likely to suffer symptoms at specified exposure levels, based on limited
evidence. Clearly, it is likely that the proportion of people who become ill will change with increasing blood lead level, but additional evidence is needed to quantify this change, particularly for population subgroups. A single adjustment factor could be adopted for all blood lead levels and for all health outcomes. It is also likely that, as the characterization of health effects improves, it will be possible to account for almost all the lead-related health effects.

Based on innumerous landmark epidemiological investigations, some of the major interventions that were adopted world-wide as a result of the global burden of disease exercise were:

- Phase-out of leaded gasoline;
- Enforcing regulations that limit:
  - Industrial emissions;
  - Worker exposure to lead in formal and cottage industries;
  - The lead content of lead-glazed pottery used for cooking, eating or drinking;
  - Lead in school materials, such as crayons;
  - The use of leaded solder in food cans;
  - The use of leaded paints;
  - Lead levels in other environmental media.

However, some of the uncertainties and lacunae in the global burden of disease exercise led to the establishment of the core requirements for public health interventions especially in developing countries like India which are:

- Routine blood lead level measurements in children and adults;
- Regular environmental exposure data for lead levels in air, water, soil and food and
Locally generated dose-response curves between blood lead levels and the possible health outcomes.

Despite the initiation in 1998 of a phase-out of leaded petrol, lead exposure in India from inhalation and ingestion of soil, dust, food and water contaminated by lead oxide (from previously combusted leaded gasoline) as well as from other environmental and occupational sources are likely to continue for a long time to come.

Further mitigation of lead exposure will require identification of sources and research clearly demonstrating the impact of continuing lead exposure on society.

Hence, the main aim of this study was to establish the current blood lead levels in children aged 3-7 years and to generate dose-response relationships between blood lead levels and the major health impacts related to the nervous system, hematological system and growth of children for the first time in India. Thus, the principle rationale behind this study was to address the major gaps in the global burden of disease exercise and help initiate public health intervention programmes.

1.2. OBJECTIVES OF THE STUDY:

- Describe the distribution of blood lead levels in children aged 3 to 7 years in Chennai city, thereby providing current exposure information on children living in a typical major metropolitan city in India.
- Determine the level of reduction in lead exposure after the phase-out of leaded gasoline in Chennai city.
- Test the hypothesis that high industry and high traffic densities will independently be associated with higher blood lead levels in children.
Test the hypothesis that higher blood lead levels will be associated with poorer performance on visual-motor, visual-spatial and fine motor functions as reflected by the Wide Range Assessment of Visual Motor Abilities Test even after adjustment for covariates like age, gender, maternal education, paternal education, birth order and anemia.

Test the hypothesis that higher blood lead levels will be associated with lower I.Q. as reflected by performance on the Binet-Kamath intelligence test even after adjusting for covariates.

Test the hypothesis that higher blood lead levels will be associated with increased risk of aggressiveness, inattentiveness, hyperactivity, anxiety and or other internalizing behaviors as reflected by the teacher rating forms of Conners’ Rating Scale – Revised, CADS – Teacher Form and Behavior Rating Inventory of Executive Function – Teacher Form.

Establish dose-response relationships between blood lead levels and the three major categories of health end-points:

* Neurobehavioral effects;
* Hematological effects and
* Effects on growth.

Identify the possible sources of lead exposure to the child from the questionnaire administered to the parent or primary caregiver.

To evaluate other published studies on impact of lead on IQ and neurobehavior of children and to relate their findings to the present study.

Finally to build models to estimate the dose-response coefficients and in particular test whether the permissible blood lead level of 10 µg/dL proposed by CDC and WHO is really “safe” for children.
1.3. PROPERTIES OF LEAD:

Lead is a dense, blue-grey, heavy, soft, malleable, non-biodegradable, metallic element that occurs naturally in the earth’s crust and is commonly used in modern industries. Some of the significant lead minerals are galena (PbS), cerussite (PbCO$_3$) and anglesite (PbSO$_4$).

Lead is a member of group IVB in the periodic table and has a melting point of 327°C. It has two oxidation states, Pb(II) and Pb(IV), in addition to its elemental stage Pb(0).

Metalllic lead is tasteless and odorless, but some of the oxides and salts of lead taste sweet, which poses a major problem, especially for children. Lead is insoluble in water, but some of the salts do dissolve, hence lead salts can be carried long distances in water supplies. Lead fumes will be easily formed when lead is heated.

As lead possesses a low melting point, heating can easily aerosolize it. Minute lead particles can travel long distances, creating problems far from their source. As human body is not capable of using lead, even small quantities of lead can lead to serious problems. Accumulation of too much of lead in the body leads to lead poisoning.

1.4. HISTORY OF LEAD:

Lead is one of the ancient metals, produced and used by humans as early as 6000 years ago in Asia Minor. Measurements of atmospheric lead deposited in arctic ice show increases around 3500 BC. This increase may be associated with heated waste from silver mining and extraction. Lead salts were extensively
used by Romans to sweeten wine. The fall of Roman Empire was also associated with such uses of lead.

Further increases in environmental lead came with the advent of the industrial revolution. However, the late 19\textsuperscript{th} and 20\textsuperscript{th} century developments contributed to a considerable extent to the environmental exposure of lead. The principle developments were the addition of lead to paint in order to improve the long-term adhesion of paint to surfaces and the use of lead as a fuel additive in leaded gasoline in 1923.

Lead poisoning has been recognized since antiquity. Eberhard Gockel, a physician in the German city of Ulm, primarily discovered lead poisoning during the Middle Ages. The effects of lead on the central nervous system were brought to light by Tanquerel des Planches in 1839. The same scientist also suggested an association between lead exposure and renal disease.

Childhood lead poisoning from lead-based paint was first described in Brisbane, Australia, in 1897. Lead poisoning was made a notifiable disease in 1899, following the pioneering work of Sir Thomas Legge. Serious concern over lead poisoning and detailed studies of the clinical and biochemical aspects of occupational lead poisoning began in 1910.

1.5. USES OF LEAD:

On a global scale, 60\% of lead is used for the manufacturing of batteries; 13\% is used in pigments and 27\% is used in the production of alloys such as solder, plastics, ammunition and a variety of other extruded products like ceramic glazes, antique-molded ornaments, storage batteries and shielding from radiation sources.
Lead has been used in plumbing for centuries. Lead, as organic compounds, is added to gasoline in order to raise the octane rating and serve as a scavenger of free radicals (antiknock agent). Small amounts of lead also may be produced from the burning of fossil fuels.

Red lead is used as a protective agent for ships, bridges, railways and various other iron and steel structures. Automobile radiator repair and scrap metal-smelting shops, as well as pewter and leaded pane manufacturing shops utilize lead.

Manufacturing of polyvinyl chloride-based plastics handle lead-containing stabilizers, including dibasic lead phthalate, lead chlorosilicate and basic lead carbonates. Cable and wire manufacturing, as well as splicing of cables utilize lead.

1.5.1. LEAD IN TECHNOLOGY:

Lead is widely used in the production of many highly technical products, right from fetal monitors to fiber optics. Lead plays a vital role in space exploration and telecommunications. NASA’s Space Shuttle uses lead-alloy solder as all the other means of connecting transistors, relays and other electronic components are not as reliable as lead. Lead alloy solders facilitate our computers to send electronic data.

Lead glazes are used to encapsulate and protect the latest generation of electronic microcircuits from atmospheric corrosion. Thus, lead-based materials play a major role in the development of hyper fast computers as well as cathode ray tubes used in viewing screens for television, computers and radar.
1.5.2. LEAD IN BATTERIES:

Batteries provide both starting power for ignition and staying power for the lights, radios and other power accessories in vehicles. Lead batteries constitute the most dependable way to store energy for future use. Lead batteries are playing a crucial role in the growing use of electric cars. Generally, the charged battery cell consists of a series of plates: the negative electrode is in the form of spongy metallic lead and the positive plate is lead dioxide. The electrolyte for this battery system is an aqueous solution of sulfuric acid.

1.5.3. LEAD IN PAINT:

Lead improves paint both as a pigment and as a binder. Lead paint “sticks” (both penetrates into and coats the painted surface) very well. Furthermore, lead is a surface biocide, and protects against some kinds of microbial overgrowth.

White lead is a basic lead carbonate; red lead is a form of lead oxide. These pigments may be used in many different color mixes. The color is not as important as the amount of lead present – up to 50% lead by weight. This is a lot of lead and it is spread as paint over a large surface area, “perfect” for creating subsequent exposure.

1.5.4. LEAD IN GASOLINE:

About 1923, a toxic liquid, tetra ethyl lead, was introduced into internal-combustion engine fuel as a gasoline anti-knock additive. It was used to increase the octane rating of gasoline by about 6 to 12 octane numbers and thus prevent pre-ignition knocking. It also served as a lubricant between exhaust valves and their seats, helping to prevent excessive wear.
1.5.5. LEAD IN MEDICINE:

Lead is an outstanding material for high-energy radiation shielding owing to its high density, capability and availability. Major progress in the medical field’s use of radiation for imaging diagnostics such as CAT (Computerized Axial Tomography) scans can be directly attributed to the use of sophisticated lead shielding to protect patients, healthcare professionals and the public. It is a principal constituent of shielding materials against ionizing radiation, including x-rays.

Lead was generally considered to have cooling properties and hence was used as a soothing lotion. Lead also found application in dentistry and was used in fillings in Europe up to the 17th century.

1.5.6. LEAD IN ART:

Some of the world’s finest china is glazed with lead, stained glass pieces such as cathedral windows are created with lead, the best stemware is made from lead crystal and thus lead is widely used to create beautiful objects of art. Statues, statuettes, figures and other such articles made of lead or lead alloys have been found from many ancient cultures.

1.5.7. LEAD IN ARCHITECTURE:

Earthquakes can cause tremendous devastation and loss of life. Japanese and US engineers are using lead in building foundations to absorb earthquake shock. Entire buildings can be mounted on platforms supported by giant springs and a series of strategically placed lead shock absorbers.
1.6. SOURCES OF LEAD:

1.6.1. IN AIR:

The use of alkyl-lead fuel additives in gasoline has resulted in widespread dispersion of lead throughout the biosphere. Combustion processes such as production of heat and electricity, primary and secondary production of lead, zinc, copper and nickel form the major sources of lead in air.

Household processes such as wood, oil and coal combustion; characteristic processes in the manufacture of other non-metallic mineral products like cement, glass, etc.; reheating furnaces of steel and iron; grey iron foundries; NPK fertilizers; pig iron tapping; basic oxygen and electric furnace steel plant; sinter plants; rolling mills; extraction and distribution of fossil fuels and geothermal energy (offshore activities – produced water, product additives and raw materials containing lead); waste incineration and pyrolysis are the medium sources of lead in air.

Manufacture of chemicals, chemical products and man-made fibres (production of paint and enamel) are the minor sources of lead in air. Humans may develop a significant body burden from inhaling airborne lead. Other pathways of airborne lead exposure include household dust and garden soil contaminated with lead from the fallout of particles present in automobile exhaust.

1.6.2. IN WATER:

Lead levels are typically low in ground and surface water, but may increase once the water enters the water distribution system. Contamination of drinking water can occur at five points in or near the residential, public school, or
office plumbing, including lead gooseneck or pigtail connectors, lead service lines or pipes, lead-soldered joints in copper plumbing throughout the building, lead-containing water fountains and coolers and lead-containing brass faucets and other fixtures.

The major sources of lead are discharges to water during primary and secondary zinc production, extraction and distribution of fossil fuels and geothermal energy and wastewater treatment.

The medium sources of lead in water include vehicle service centers and petrol stations, laboratories, characteristic processes in the mining and quarrying industry, except for energy producing materials, calcium carbide production, and solid waste disposal on land.

The minor sources of lead in water are manure management, including mineral fertilizers, processes specific to hunting and aquaculture, inland waterways and maritime activities (professional and recreational navigation, grease from propeller shafts), construction and demolition (roofs, gutters), household consumption and similar processes (batteries and other lead containing products), paint application, combustion processes (production of heat and electricity), manufacture of chemicals, chemical products and man-made fibers, characteristic processes in the manufacture of other non-metallic mineral products (cement, glass, etc.), NPK fertilizers, phosphate fertilizers, waste incineration and pyrolysis, contaminated sediments, sites and soils.

1.6.3. IN SOIL:

Lead in soil is mainly due to the settling in of lead dust present in air and the run-off from the nearby water sources. Hence the major sources of lead in soil would be similar to those in air and water.
1.6.4. IN FOOD:

Contamination can be introduced by canning, by use of food supplements rich in lead, or by ingestion of contaminants containing lead. Under poor conditions, lead leaches from metal or solder in food containers. By far the greatest oral source of lead is ingestion of either paint chips or dust that contains paint. Paint chips can contain 40% (400,000 microgram/g) or even more lead by weight.

1.6.5. OCCUPATIONAL AND ENVIRONMENTAL EXPOSURE:

Inhalation and ingestion are potential routes of lead exposure in mining, particularly the more soluble carbonate and sulfate ores. Grinding and sintering operations generate high levels of lead dust and fumes. Workers engaged in the reclamation of lead from secondary sources have potential exposure to lead as well as other metal contaminants. Exposure is a constant hazard in the manufacture of lead batteries. Paint and pigment manufacturers are exposed to lead, especially during fine spray-painting operations. Torch burning to remove lead-based paints generates significant quantities of lead fumes. Welders and brazers may be exposed to lead alloys, fluxes and coatings. Workers in munitions plants and rifle ranges may have exposure to lead dust, particularly indoors. Glassmakers, artists and pottery workers may unknowingly be exposed to high levels of lead in pigments and glazes.

Other occupations which may involve exposure to lead include abrasive blasters, acoustic and heating insulation installers, aircraft repair, air conditioning/heating fitters, aerial installers, alarm installers, ammunition manufacture, architects, asbestos removers, automotive body or radiator repair and maintenance, boat builder, brass or copper foundry, bricklayers, bridge,
tunnel and tower workers, builders, building inspectors, cabinet makers, cable layers, cable repair (telephone and other lead shielded cables), carpenters/joiners, carpet traders, chemical preparation, concrete traders, construction and renovation workers, demolition workers, electricians, engineers, excavators, firing range staff, landscapers, lead smelter, production and refining, miners, paint, pigment or shellac manufacturers, petrol station workers, plumbers/pipe fitters, recycling facility workers, rubber manufacturers, scrap metal recovery workers, stone masons, tillers, waterproofing specialists and wall paper contractors.

1.6.6. OTHER SOURCES OF LEAD:

Folk remedies and cosmetics of certain ethnic groups sometimes contain lead. Ayurvedic metal-mineral tonics have been identified as a potential source of high lead. Lead has also been found in the wicks of certain kinds of candles.

1.7. RISK GROUPS:

Children aged 9 months to about 5 years are most at risk because they crawl on the floor, breathe in a zone nearest the floor, get lead on their hands during floor contact activities, and engage in hand-mouth activities (pica) most commonly.

Moreover, children inhale a greater volume of air in relation to body mass than adults. The rate of deposition of lead in children is considerably greater than in adults.

Pregnant women are also at risk. At the time of pregnancy, due to calcium deficiency, lead tends to be released from the maternal bones and get accumulated in the maternal blood which can be transferred to the fetus, as the
fetal blood-brain barrier is incompletely formed and lead can accumulate in the fetal central nervous system far faster than in the maternal central nervous system. Fetal hemoglobin also appears to have a greater affinity for lead than adult hemoglobin. For women, menopause may be another time of vulnerability; for example, there is strong evidence that at the time of menopause, blood lead levels increase because of liberation of stored lead from bones.

1.8. ROUTES OF ENTRY:

Lead is usually encountered by inhalation or oral ingestion. Respiratory exposure is more commonly the primary route in adults, while ingestion is often most important in children. Lead is absorbed and distributed to other parts of the body via the bloodstream.

Once absorbed, lead is distributed in essentially the same manner regardless of the route of entry.

1.8.1. INHALATION:

Some fraction of inhaled air-borne lead is deposited in the respiratory tract. The rate of deposition of particulate air-borne lead in adult humans varies from 30 to 50%. Once deposited in the lower respiratory tract, lead is almost completely absorbed. Approximately 30 to 40% of the amount of tetra alkyl lead inhaled in vapor is absorbed by the lungs.

1.8.2. INGESTION:

Adults absorb about 8 to 15% of ingested lead. Fasting adults absorb more. Children absorb 30-50% of ingested lead, and more, if fasting or malnourished. Pregnant women are also likely to absorb lead more efficiently.
Children and pregnant women are supporting bone development. Lead is more likely to be absorbed when the gut is “primed” to absorb Fe++ and Ca++.

1.8.3. DERMAL:

Skin is relatively impervious to lead, lead oxides, or lead salts. Some may get through scrapes or wounds, but organic leads, such as in leaded gasoline, will go through skin into the bloodstream quite well. Like many organic metals, alkyl leads are readily absorbed through the skin. In addition, they are taken up into organs more rapidly. They are very dangerous.

1.9. METABOLISM:

Inhalation and ingestion are the primary routes of absorption of lead compounds. Approximately 40% of inhaled lead oxide fumes are absorbed through the respiratory tract. Absorption of particulate lead dust from the lungs depends on particle size and solubility. Particles in the 0.5-5.0 micron range are most likely to be deposited in the alveoli where they can be absorbed. Larger particles, which are entrapped in the larger airways, are likely to be swallowed and may lead to gastrointestinal absorption. Roughly 5-10% of ingested lead compounds are absorbed from the gastrointestinal tract. Iron and calcium deficiencies and high-fat diets may increase the gastrointestinal absorption of lead. Gastrointestinal absorption is greater in infants and children than in adults.

In the bloodstream, the majority of the absorbed lead is bound to erythrocytes (Fig. 1). The free diffusible plasma fraction is distributed to brain, kidney, liver, skin and skeletal muscle, where it is readily exchangeable. The concentrations in these tissues are highest with acute, high-dose exposure. Lead crosses the placenta, and fetal levels correlate with maternal levels. Bone constitutes the major site of deposition of absorbed lead, where it is incorporated.
into the bony matrix similar to calcium. The lead in dense bone is only slowly mobilized and gradually increases with time.

Fig. 1: A compartmental model for lead biokinetics, with multiple pool for blood lead

Intracellularly, lead binds to sulfhydryl groups and interferes with numerous cellular enzymes, including those involved in heme synthesis. This binding accounts for the presence of lead in hair and nails. Lead also binds to mitochondrial membrane and interferes with protein and nucleic acid synthesis. Excretion is slow over time, primarily through the kidney. Fecal excretion, sweat and epidermal exfoliation are other routes of excretion. The half-life of lead is long, estimated to be from 5 to 10 years. This varies with the intensity and duration of exposure and the ultimate body burden accumulated. Bone diseases (osteoporosis, fractures) may lead to increased release of stored lead and elevated blood lead levels.
Water-insoluble alkyl lead compounds are readily absorbed through intact skin. Respiratory and gastrointestinal absorption are significant as well. Tetraethyl and tetramethyl lead are converted to the trialkyl metabolites that are responsible for toxicity. The fat solubility of these compounds accounts for their accumulation in the central nervous system. Alkyl lead compounds are ultimately converted to inorganic lead and are excreted in the urine.

Adults consume approximately 30 microgram of lead each day, of which only 10% is absorbed. The daily respiratory intake is probably about 15 to 20 microgram. Unlike adults, children absorb about 50% of ingested lead. A single chip of paint the size of a thumbnail can contain 50 to 200 mg of lead; the consumption of a few such chips a day equals 1000 times the allowable intake for an adult.

Humans may develop a significant body burden from inhaling airborne lead. Inhaled lead aerosols, like other particles, are deposited in the lung by diffusion, sedimentation and impaction. About 20 to 60 percent of inhaled lead particles are deposited in the adult human respiratory tract. The amount of deposition varies with rate and depth of respiration, age and sex of the person, which determines the size of the airways.

1.10. HEALTH EFFECTS OF LEAD:

Lead is one of the oldest-established poisons. Knowledge of its general toxic effects stretches back three millennia and knowledge of its effects in children over hundred years. Depending on the exposure levels, lead is said to have both mild and adverse effects on the nervous system, peripheral nervous system, growth and development, cognitive development, behavior, hearing, sight, movement and muscular activities, digestive system, excretory system, blood and circulation. In severe lead poisoning, it can also lead to death.
1.10.1. CLINICAL FEATURES OF LEAD POISONING:

Lead poisoning most commonly presents as abdominal pain. It may mimic peritonitis because of its intensity and association with a rigid abdominal wall. This has been termed lead colic. Other gastrointestinal symptoms include constipation, vomiting and anorexia. Less commonly, peripheral neuropathy involving paralysis of frequently used muscle groups is present. Lead encephalopathy may manifest as seizures, coma or stupor or a variety of other complaints including confusion and headaches.

Symptomatic lead poisoning in childhood generally develops at blood lead levels exceeding 80 µg/dL and is characterized by abdominal pain and irritability followed by lethargy, anorexia, pallor (resulting from anemia), ataxia and slurred speech. Convulsions, coma and death due to generalized cerebral edema and renal failure occur in the most severe cases. Subclinical lead poisoning (blood lead level > 30 µg/dL) can cause mental retardation and selective deficits in language, cognitive function, balance, behaviour and school performance despite the lack of discernible symptoms.

In adults, symptomatic lead poisoning usually develops when blood lead levels exceed 80 µg/dL for a period of weeks and is characterized by abdominal pain, headache, irritability, joint pain, fatigue, anemia, peripheral motor neuropathy and deficits in short-term memory and the ability to concentrate. A “lead-line” sometimes appears at the gingival-tooth border after prolonged high-level exposure.

Chronic sub-clinical lead exposure is associated with interstitial nephritis, tubular damage, hyperuricemia and a decline in glomerular filtration rate and chronic renal failure. Epidemiologic evidence also suggests that blood lead
levels in the range of 7 to 35 µg/dL are associated with increases in blood pressure, decreases in creatinine clearance and decrements in cognitive performance that are too small to be detected as a lead effect in individual cases but nevertheless may contribute significantly to the causation of chronic disease.

1.10.2. EFFECTS ON HEME BIOSYNTHESIS:

One of the most important mechanisms of lead toxicity is its effect on various enzymes in the heme biosynthetic pathway. Lead interferes with heme biosynthesis by altering the activity of three enzymes: delta-aminolevulinic acid synthetase (ALA-S), delta-aminolevulinic acid dehydrase (ALA-D) and ferrochelatase. Lead stimulates the mitochondrial enzyme ALA-S, which catalyzes the condensation of glycine and succinyl-coenzyme A to form delta-aminolevulinic acid (ALA).

Lead directly inhibits the cytosolic enzyme ALA-D, which catalyzes the condensation of two units of ALA to form porphobilinogen. Hence, the inhibition of ALA-D and feedback derepression of ALA-S result in accumulation of ALA. Lead also decreases the activity of the mitochondrial enzyme ferrochelatase, which catalyzes the insertion of iron (II) into the protoporphyrin ring to form heme. This results in the accumulation of protoporphyrin IX, which is present in the circulating erythrocytes as zinc protoporphyrin (ZPP), due to the placement of zinc, rather than iron, in the porphyrin moiety.

Thus, a marked interference with heme synthesis results in a reduction of the hemoglobin concentration in blood. Decreased hemoglobin production, coupled with an increase in erythrocyte destruction, results in a hypochromic, normocytic anemia with associated reticulocytosis.
Fig. 1: Multiorgan impact of reductions of heme body pool by lead: impairment of heme synthesis by lead results in disruption of a wide variety of important physiological processes. Source: EPA 1986a
The impact of impairment of heme synthesis by lead is not limited only to the hematopoietic system. It results in disruption of a wide variety of important physiological processes. The reduction of heme body pool leads to erythropoietic, neural, renal endocrine and hepatic effects which are explained in Fig. 2.

1.10.3. ERYTHROCYTE DESTRUCTION:

Lead is said to inhibit the activity of the enzyme pyrimidine-5’-nucleotidase, which results in the accumulation of pyrimidine nucleotides in the erythrocyte or reticulocyte, thereby affecting the stability of the erythrocyte membrane.

1.10.4. NEUROLOGICAL EFFECTS:

Of the several organ systems affected by lead, the nervous system is particularly sensitive to its effects. Chronic low-level lead exposure may cause neurologic impairment, including decreased intelligence, behavioral and learning disorders and deficits in visuomotor function, perceptual integration and verbal abstraction.

Overt manifestations of lead-related encephalopathy include ataxia, confusion, convulsions, fatigue and mood-changes. Exposure to inorganic lead has resulted in characteristic changes in behavior and cognitive functioning in patients with blood lead levels less than 70 µg/100ml.

As lead levels rise about 40 µg/100ml, short-term verbal memory skills have been found to be consistently impaired. Lead exposure in the range of 90 µg/100ml can lead to impairment in attention, psychomotor function, verbal concept formation, short-term memory and visuospatial abilities. Mood disorders
resulting in apathy, irritability and diminished ability to control anger are apparently common.

The characteristic “wrist drop” has been considered pathognomonic of the diagnosis of lead poisoning. Recent studies of probable adult lead neuropathy describe progressive generalized weakness, mild distal atrophy, reflex loss and occasional fasciculation. Lower limb weakness is prominent in childhood cases. In lead intoxication, motor nerve conduction velocity is affected more than sensory nerve conduction velocity because the toxic effect involves segmental demyelination and remyelination.

1.10.5. GASTROINTESTINAL EFFECTS:

Gastrointestinal symptoms consist of epigastric discomfort, nausea, anorexia, weight loss and dyspepsia. At high blood lead concentrations, usually much above 80 μg/dL, these nonspecific symptoms may be accompanied by severe intermittent abdominal cramps known as lead colic. During a severe attack of colic, the patient’s blood pressure is frequently elevated, with a concomitant bradycardia. The direct action of lead on visceral smooth muscle tone and vagal irritation associated with intestinal ischemia is the underlying pathology for lead colic.

1.10.6. RENAL TOXICITY:

1.10.6.1. ACUTE LEAD NEPHROPATHY:

Acute lead nephropathy is associated with severe acute lead poisoning, characterized by colic, encephalopathy, peripheral neuropathy and anemia. Renal findings include Fanconi’s syndrome, a proximal tubular reabsorption defect characterized by aminoaciduria, glycosuria, hyperphosphaturia, and
hypercalciuria. It has become evident that tubular proteinuria accompanies these proximal tubular reabsorptive defects. Mitochondrial destruction is prominent in this stage. The mitochondria are swollen and distorted in shape.

1.10.6.2. CHRONIC LEAD NEPHROPATHY:

Glomerular filtration rate and effective renal plasma and blood flow rate are reduced. Typically, renal failure is evident only after years of intense exposure and is frequently associated with hypertension and gout. In chronic lead nephropathy, the kidney shows the characteristic morphology of relatively acellular tubulointerstitial nephritis. The appearance of arteriolar nephrosclerosis before hypertension and the relatively short duration of hypertension preceding renal failure suggest that the primary injury from lead is to the renal microvasculature.

1.10.7. ENDOCRINE EFFECTS:

Adrenal steroid excretion was first found to decrease and then to increase considerably during advanced stages of lead intoxication. Aldosterone secretion rate and plasma rennin activity were depressed. Thyroid function was depressed because of decreased uptake of $^{131}$I.

1.10.8. REPRODUCTIVE EFFECTS:

Occupational exposure to lead, both maternal and paternal, has historically been associated with decreased fertility, spontaneous abortion, stillbirth, low birth weight, prematurity, abnormal CNS development, behavioral abnormalities, varied minor congenital malformations and increased infant mortality. At one stage, lead was even used to induce abortions (Hall and Cantab, 1905).
Lead readily passes the placenta and accumulates in the fetus and there is strong evidence that a mother’s lead burden can cause serious effects on cognitive development of her child. High maternal lead exposures cause spontaneous abortion and stillbirth. At lower doses, children exposed in utero are of lower birth weight and are more likely to have neural tube deficits. They may develop neuropsychiatric syndromes similar to those exposed early in childhood.

The other outcomes of lead exposure in females include menstrual disorders, reductions in the number of corpora lutea and formation of ovarian follicular cysts. The outcomes of lead exposure in males include detrimental effect in motility, morphology, count and functional maturity of sperms; peritubular testicular fibrosis and decreased prostate vesicle function.

**1.10.9. MYOCARDIAL EFFECTS AND HYPERTENSION:**

Degenerative changes in heart muscle have been found in lead poisoned children. Cardiac lesions and electrocardiographic abnormalities are also seen in some cases. In various population studies blood lead concentrations in adults have been associated with increased blood pressure. Significant increases in systolic and diastolic blood pressure were associated with increasing blood lead levels.

**1.10.10. EFFECTS ON IMMUNE SYSTEM AND GROWTH:**

Lead suppresses the levels of secretory IgA (Immunoglobulin A) which is a major factor in the defense against respiratory and gastro-intestinal infections. Lead also suppresses the release of thyrotropin – stimulating hormone in response to thyrotropin – releasing hormone.
1.10.11. GENETIC POLYMORPHISMS:

Occupational exposure of lead is associated with increased mitotic activity in peripheral lymphocytes, increased rate of abnormal mitosis and increased incidence of chromosomal aberrations.

Trimethyl and triethyl lead were associated with increased frequency of induced sister chromatid exchanges and altered chromosome length in cultured human lymphocytes.

Lead uptake, absorption and metabolism have been found to be involved in the occurrence of a variety of polymorphic genes like genes that code for aminolevulinic acid dehydratase (ALAD), the apolipoprotein E family (APOE), hemochromatosis (C282Y, H63D) and the Vitamin D receptor (VDR).

1.11. CONCLUSION:

Although lead has many useful characteristics, the health effects from exposure are serious. Knowledge and awareness of the problem are essential to limit the risk of lead exposures. The reduction of lead in air greatly reduces exposure through inhaled air and swallowed dust, food, water and beverages contaminated with lead deposited from air. However, some lead exposure will continue to occur, owing to background exposure resulting from natural sources of lead and to past deposition of lead onto soil and into other media from which it can get into the human food chain. Lead will continue to be an important public health concern despite the discontinuance of its use as a gasoline additive and hence a comprehensive awareness of the possibility of lead poisoning is critical to timely diagnosis.