AKNOWLEDGMENT

I wish to express my deepest thanks and gratitude to Dr. Shadia Abd-El Hamid Fathy Prof. of biochemistry, Faculty of science, Ain-shams University for her interest and co-operation.

I am deeply grateful to Dr. Abd-El Baset, M.S Prof. of biophysics, National Research Centre, for suggesting the problem, valuable assistance and constructive critisim through this thesis.

The author is greatly indebted to the National Research Centre for the Financial support and facilities that enabled us to carry out this work

ABBREVIATION AND ALTERNATIVE TERMINOLOGY

ALA: Aminolevulinic Acid
d-ALA /δ - ALA: Delta Aminolevulinic Acid
δ - ALA-D: Delta Aminolevulinic Acid Dehydratase
δ - ALA-δ: Delta Aminolevulinic Acid Synthetase
U - ALA: Urinary Aminolevulinic
ATP: Adenosine Triphosphate
BAL: British - Anti Lewisite
B.S.E: Basophillic Stippled Erythrocyte
Ca^{++}: Calcium ion
Cd: Cadmium
C.N.S: Central Nervous System
Cp: Coproporphyrinogen
U- Cp: Urinary Cp
Cu^{++}: Copper ion
D.N.A: Deoxribonucleic Acid
DMSA: Dimercapto - Succenic Acid
E. S - ALA-D: Erythrocyte, delta ALA-D
EDTA: Eythelene diamine tetra acetate
ECG: Electrocardiogram
EPP: Erythrocyte, Protoporphyrin
FAO: Food Agriculture Organization
Fe: Iron
GABA: Gamma Amino Butyric Acid
SALT: Serum Alanine Aminotransferase
SAST: Serum Aspartate Aminotransferase
GSA: Glutathione - S - Adenosine
Hb: Hemoglobin
HbA: Adult Hemoglobin
HbA$_1$: Glycosylated Hemoglobin
HbA$_{1c}$: Fraction of glycosylated Hb.
Co - Hb: Carboxy Hb.
Hb - F: Fetal - Hb.
Hb - O$_2$: Oxy - Hb.
S - Hb: Sulf - Hb.

بسم الله الرحمن الرحيم

Hg : Mercury
ISDW : International Standard for Drinking Water
I.U. : International Unit
K^{++} : Potassium ion
LCAT : Lecithin : Cholesterol Acyl Transferase
mM : milli Molar
MAO : Mono Amino Oxidase
MCV : Mean Corpuscular Volume
MDI : Mean Dieatery Intake
Mg : Magnesium
MFA : Mercopto Furyle Acrylic Acid
Na - K - ATPase : Sodium - Potassium ATPase
NADP : Nicotinamide Adenine Dinucleotide Phosphate
ng : nanogram (10^{-9})
NHANES : National Health and Nutrition Examination Survey.
Met - Hb : Met - hemoglobin
P^{+3} : Inorganic Phosphorus
Pb : Lead
PbB : Blood lead
PH : Log of the reciprocal of the hydrogen ion concentration
P-5' - N : Pyrimidine 5' nucleotidase
P.P : Protoporphyrin
PPm : Part per million
PPb : Part per billion
RBC : Red Blood Cell
RCC : Red Cell count
Sn : Stunus
TEL : Tetra Ethyl Lead
TML : Tetra Methyl lead
TSH : Thyroid - Stimulating Hormone
μg/dl : Micro gram /deciliter
WHO : World Health Organization
Zn : Zinc
ZPP : Zinc protoporphyrin

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The effects of lead exposure on various organs and systems is discussed pathologically in term of dose effects and environmentally as dose - response.

Dose effect refers to the relationship between dose and the intensity of a specified effect in an individual, while dose-response refers to the relationship between the dose and the proportion of a population showing a defined effect, specified as the level of intensity. The organs which are mainly affected in long term low doses of lead exposure are the hemopoietic system, nervous systems, renal system, cardiovascular system and to a lesser extent liver, endocrinal glands and reproduction (Hernberg et al., 1970; Granick et al., 1973).

Inorganic lead Causes contraction of the peripheral vascular system and affects the blood forming tissues i.e. the bone marrow. Almost in all cases of lead exposure, hemopoietic changes appears before onset of signs and symptoms, also they provide quantitative information on lead exposure. These hemopoietic changes are mainly secondary to the effect of lead on the normal pathway of hemoglobin synthesis (Cramer et al., 1975).

In addition chronic lead nephropathy is associated with arteriosclerotic changes, interstitial fibrosis, glomerular atrophy, and hyaline degeneration of the vessels. This progressive disease sometimes ends in renal failure (Cramer et al., 1975). Under condition of long-term exposure arteriosclerotic changes have been demonstrated (Torres et al., 1968). In many cases the ECG abnormalities disappeared with chelation therapy, suggesting that lead may have been the original etiological factor (Sliver and Torres, 1968).

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Little impairment of the thyroid function and adrenal function has been reported in cases of lead poisoning (Sandstead et al., 1970). Also, there is some evidence suggesting that lead may cause some derangement of tryptophan metabolism (Dugandzic et al., 1973).

The literature is controversial as regards chromosomal abnormalities induced by exposure to lead. Thus the question as to whether chromosomal abnormalities occure as a result of lead exposure in man remains open.

The aim of this work is to study the disturbances of hemoglobin dynamic motion to determine the threshold turning point which refers to the irreversible changes. Therefore, the following items must be studied to overcome the requirements :

- Study the changes of electronic structure of heme in different lead intoxication.
- Study the dynamic motion of hemoglobin which involves the dynamic folding after being unfolded.
- Study the different derivatives of HB.
- Study the effect of lead intoxication on HB. pattern
- The bioenergetic of HB. as a biomolecule.
- Study the oxidation - reduction system of HB.
- Magnetic succeptibility and magnetic moment.
- Study the effect of lead toxicity on liver - kidney functions.

This study could provide or even highlights the early signs of diagnosis on molecular level and the way of treatment.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Physical and Chemical Properties of Lead

Lead is a bluish or silvery-grey soft metal of atomic number, 82; atomic weight, 207.19 specific gravity, 11.34. The melting point is 327.40°C and the boiling point, at atmospheric pressure, is 1740°C . With the exception of the nitrat, the chlorate, and to a much lesser degree, the chloride, the salts of lead are poorly soluble in water and soluble in dilute nitric acid. It has four naturally occurring isotopes : 208, 206, 207 and 204 in order of abundance. The isotopic ratios for various mineral sources are sometimes substantially different. This property has been used to carry out non radioactive tracer environmental and metabolic studies (Elkins, 1959; WHO, 1977).

Although lead has four electrons in its valence shell, only two ionize readily. The usual oxidation state of lead in inorganic compounds is therefore, +2 rather than +4.

Lead is mined most usually as sulphide "galena". Other important inorganic compounds are lead monoxide "Litharge", lead carbonate, sulfate, arsenate, chromate, chlorophosphate and chloride. Metals such as antimony, arsenic, bismuth and tin may be added to lead to improve its mechanical or chemical properties. Lead itself may be added to alloys such as bronze, brass and steel to obtain certain desirable characteristics (Elkins, 1959).

Lead uses

- Modern consumer use of lead throughout the industrialized world has more than doubled during the last 30 years. The annual consumption in the united states alone is well above one million tons or about 10 Ibs/ inhabitant. The storage battery industry is one of the largest single users of lead (about 40%). The second largest consumer is the petroleum industry, which was about 20% in producing lead alkyls as gasoline additive.

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Lead in the form of tetraethyl & tetramethyl lead and mixed lead alkyls are used as an antiknock additive to improve the combustion characteristics of gasoline. It is used in the form of sheets or pipes where pliability and resistance to corrosion are required such as in chemical plants and building industry. It is used also for cable sheathing, as an ingradient in solder, and as a filler in the automobile industry. It is a valuable shielding material for ionizing radiations.

About 35% of lead is used as organic and inorganic chemical compounds. Lead oxides are used in the plates of electric and accumulators, in rubber manufacture (lead monoxide (pbo) and used as constituents of glazes, enamels and glass.

Lead salts form the basis of many paints (most such paints were recently banned in the United States) and pigments. lead carbonate and lead sulphate are used as white pigments. Lead arsenate is an insecticide.

In printing, molten lead is used to form printing figures by composing machines. Letters of press are formed of lead alloy, which is composed mainly of lead with a small percentage of antimony and tin. lead which would be too soft if used alone, forms the body for the type metal, constitutes 84% of alloy. Antimony gives hardness to lead alloy, it constitutes 12% of alloy. Tin adds toughness to the type metal and makes it possible to cast at much lower temperature, it constitute 4% of alloy (Ralph and Edwin , 1964).

LEAD IN THE ENVIRONMENT :

Lead poisoning has been recognized since antiquity. The ingestion of beverages containing lead leached from highly soluble glazes or earthen ware containers, the distillation of alcohol in leaded flasks is another rare cause of plumbism in certain areas, although the practice was prohibited in (1723) by the Massachustes Bay colony after it was noticed that consumption of rum so distilled resulted in abdominal pain known as the dry gripes (**Klein, 1970**).

- Chronic lead - poisoning was a major cause of illness throughout the period of the Roman Empire. It was widely used in dishes and coins and to transport water. Its use declined with the fall of the Roman Empire but accelerated with the onset of the industrial revolution.

Today lead is a ubiquitous element present in the food we eat, the water we drink and the air we breathe, lead aerosol is a common air contaminant. It is evident that in the past two decades, man's continuing use of lead has resulted in an environment level far above that which would exist naturally and that this could have grave consequences in human health.

Sources of lead :

Lead (pb) is a natural constituent of soil, water, vegetation, animal life, and air, although the levels of the natural concentrations are not certain. Significant sources of naturally occurring lead include dust from soils and particles from volcanoes. In contrast to certain other metals such as mercury, lead in its elemental form is not believed to be a major source of poisoning.

1- Air :

In rural areas levels of lead in air of 0.1 $\mu g/m^3$ or less are found. However, depending upon the degree of pollution due to urbanization, the amounts of lead in city air range from 1 to 3 $\mu g/m^3$ and will occasionally be much higher under peak traffic condition (Ludwig et al., 1965). On the basis of the information before the committe; and depending upon the degree of urbanization of the area concerned, its topographical situation, weather conditions and habitat, it may be assumed for the purposes of this report that the intake of lead by inhalation in cities could on occasion be 100 µg/day. Lead containing dusts are present in many manufacturing processes and may add to the lead content in all foods to a small degree (Shy et al., 1971). The pb- level in dust was directly related to traffic density, (Lee et al., 1988).

A source of lead that calls for particular consideration is the lead tetra - alkyls used as petrol (gasoline) additives. Tetra ethyl lead and tetra methyl lead known as anti-knock agents. In the internal combustion engine, the pb - tetra alkyls are oxidized, and the committee did not consider that the intake of alkyl lead as such was significant. Since only negligible amounts of the lead alkyls in the gasoline are exhausted directly into the atmosphere, it is unlikely that the health of the general public would be affected (Hirschler and Gilbert, 1964). However, the lead derived from petrol additives contributes not only to the intake through inhalation but also to the intake through ingestion as a result of fallout from vehicle exhausts on nearby food crops.

The lead exhausted by automobiles originates in the antiknock fluid in the gasoline. The fluid contains lead alkyls & organic scavengers, ethylene dichloride and dibromide, whose function is to combine with the lead to form inorganic lead salts. The chemical composition of exhaust particles from internal combustion engines appears to be related to particle size. The major lead products emitted in particles of 2-10 µm equivalent diameter are lead bromochloride (PbClBr) and the alpha & ß forms of ammonium chloride and lead bromochloride (NH_4Cl ; 2PbClBr) together with minor quantities of lead sulphate and mixed oxide (Pbo; $PbBrH_2o$). The particles subsequently lose halogens (process which appears to be photochemically enhanced) and become smaller and more soluble (especially in the presence of So_2). Several reports have suggested that lead halogen compounds are then converted to Oxides and / or carbonates. The amount of lead discharged to the atmosphere in the exhaust gases varies, depending on driving conditions, from about 25% to above 75% of the pb intake in the fuel. At low speeds the pb tends to be retained in the exhaust system & is discharged at some later period when the engine is run at greater speeds.

The level of atmospheric pb varies directly with the volume of traffic and size of the community (Daines et al., 1970) Los Angeles, with a population of more than 2.5 million, has the highest concentration of the communities studies, with a mean of approximately 5 µg/m^3 air. Other urban communities with a population greater than 2 million have values of about 2.5 µg. Communities that are smaller than a million have a mean atmospheric concentration of about 2 ug, & Communities with a population of less than 100.000 have a mean value of about 1.7 µg, (Cholak, 1964). The mean is today on the rise by as much as 5% per year and week - long averages of 8 µg now occur in San Diego, (Chow and Earl, 1970).

An increased lead content may be founds in crops at distances up to 50 metter from highways, depending on weather conditions and traffic volume (Motto et al., 1970). Although formely significant, the atmospheric contribution to total lead levels from fossil fuels is now negligible compared with that from lead containing petrol additive.

Some unconfirmed reports have suggested that a very small proportion of the total pb in urban air might be in organic form. This is a separate problem that needs to be considered by experts in air pollution. The contribution of pb from air to total intake can be estimated solely from the total body burden. The total pb absorbed daily was considered to be the sum of the amounts absorbed from the diet and from the air (It was assumed that the total dietary (food plus water) lead was constant at 200 µg/day (Rabinowitz et al., 1976) and that 8% of this dietary lead or 16 ug, was absorbed. The remainder of the amount absorbed was distributed to air - lead (Fig. 1).

The amounts of lead in each compartment, exchanging daily between compartments, and excreted daily are shown for steady state conditions of continuous exposure to food, water, and air lead. The amounts of lead shown entering the central compartment in each case are the amount that assumed to be absorbed daily into the systemic circulation from all sources.