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RESEARCH ARTICLE

MECHANISM AND TOXIC EFFECTS OF SOME HEAVY METAL ON HUMAN HEALTH

Dr. Renu Saraswat¹, Dr. Devesh Saraswat² and Dr. Nupur Chatterji¹

1. Associate Professor, Department of Chemistry, Meerut College, Meerut.
2. Lecturer, Department of Chemistry, Eicher School, Faridabad.

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Abstract

The most promising challenge of developing industries is the release of heavy metals in the environment. Though there have been much efforts made during past decade to eliminate the release of these metals by the developed countries yet the risk is increasing continuously as these metals can neither be destroyed nor can be recycled easily. Moreover use of new therapies for the cure of many carcinogenic diseases and neurogenetic disorders also require the consumption of heavy metals in one form or other. Because of a high level of toxicity heavy metals like arsenic, mercury, lead, chromium and aluminium are of primary concern for public health. Toxic effect that can be caused by these heavy metals depends mainly upon amount of dose consumed, the route of vulnerability and length of exposure to the heavy metal i.e. severe or persistent. Toxicity caused by these metals can lead to oxidative stress due to the genesis of free radicals and may result in excessive health hazards. This review article aims to discuss the sources of exposure, mechanism of toxicity, health effects along with some common diseases caused in human by these heavy metals.

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Introduction:-

Metals may be defined as substances which are good conductors of heat as well as of electricity and possess metallic lustre. Metals are also known to possess certain mechanical properties like high tensile strength, malleability and ductility. The distribution of metals in environment is controlled by various characteristic properties of the metal and by a number of environmental components (1). Metals may be broadly classified into light and heavy metal in terms of their density. Density of Light metals like Li, K, Na, Ca etc is less than 5 gm/cm^3 whereas density of heavy metals like Sn, Pb, As, Hg is more than 5 gm/cm^3 . Among the known metals Li (density $.53 \text{ gm/cm}^3$) is lightest and Os (density 22.5 gm/cm^3) is heaviest metal.

Heavy metals are naturally present in earth's crust and are used for various industrial objectives. Heavy metals like iron, lead, mercury, copper etc are the indicators of human progress. Heavy metals are considered to be the mainstays of all major civilizations. One can not imagine to travel, compute or perform any important task of life without the support of these metals.

S.No	Nontoxic	Low toxic	Moderately toxic	Highly toxic
1	Aluminium	Tin	Antimony	Uranium
2	Bismuth	Scandium	Beryllium	Vanadium

Corresponding Author:- Dr. Renu Saraswat

Address:- Associate Professor, Department of Chemistry, Meerut College, Meerut.

3	Calcium	Barium	Boron	Zinc
4	Iron	Germanium	Actinium	Zirconium
5	Magnesium	Gold	Cadmium	Tungsten
6	Manganese	Erbium	Chromium	Radium
7	Lithium	Gallium	Hafnium	Ruthenium
8	Sodium	Holmium	Copper	Thorium
9	Rubidium	Neodymium	Indium	Thallium
10	Strontium	Terbium	Lead	Titanium
11	Potassium	Thulium	Mercury	Silver
12	Molybdenum	Tin	Nickel	Polonium
13		Ytterbium	Platinum	
14		samarium	Palladium	

Table:- classification of heavy metals based on toxicity.

(Source: U.S. GEOLOGICAL SURVEY 1133, 1995)

On the other hand heavy metals are also considered to be the environmental pollutants of major concern because like most other organic pollutants metals are non- biodegradable or perishable. Among the 35 natural occurring metals 23 metals have high specific density i.e more than 5 g/cm^3 and their atomic weight more than 40.04 and possess similar physical and chemical properties (2,3).A few of the heavy metals have functional roles necessary for a number of physiological and biochemical activities of human body when taken in an adequate amount . At the same time these heavy metals exert harmful effect when taken in high amount whereas some others are delirious to human body even if it is taken in small doses and may result into acute and lifelong toxicity . Out of these 23 metals lead (Pb), mercury (Hg) and cadmium (Cd) do not have any biological importance to human body and are known for their extremely toxic effect. Other toxic metals are chromium, copper, manganese, nickel, tin and zinc.

These heavy metals once they are absorbed they remain in the body of a human being for infinite time and do not get degraded .After accumulating at a higher concentration they result in the formation of complexes within various tissues and cells thereby causing a number of diseases (4).

Sources of exposure and mechanism of toxicity of heavy metals

Toxic heavy metals are released into the environment through the municipal and organic wastes , mining, chemical ,electric and leather industries , process of smelting as well as refining of metals ,burning of fossil , vehicular exhaust, thermal power plants ,fertilizers and agricultural wastes. These heavy metals can be transported from place to place by wind depending upon the fact that they are present in gaseous phase or in the form of particulate matters ,by erosion or by acid rain to various loctaions on soils and water bodies . Heavy metals are present everywhere in air we breathe in food that we consume and in water we drink. Although everywhere in the ecosystem these heavy metals are present but their exposure to the humans is through various man made activities. Unlike organic pollutants heavy metals are indestructable poisons. Even a small concentration is capable of disrupting bodys normal metabolism. Exposure to heavy metals can repress the immune system by increasing the toxicants in body (5).

Human being are exposed to the toxic effect of the heavy metals present in environment if they inhale the air adulterated with the dust of metal particles , smoke and small molecule produced by ignitions, consuming contaminated food , eating at the polluted place without washing hands. On intake, the heavy metals become integral part of some body parts like bones. Kidney, liver, brain and accumulate with many years half-life (6).Sources and mechanism of toxicity of some of the harmful heavy metals are discussed below.

Arsenic

Arsenic is a metalloid and it does not exist in nature in free form but is present as a compound in combination of oxygen, chlorine ,hydrogen ,lead or mercury.The two soluble inorganic forms of arsenic are arsenite (trivalent state As^{3+}) and arsenate (pentavalent state As^{5+}) .Their Compounds are lethal to human beings and other organisms present on the earth. Arsenite is hundred times more toxic in comparison to arsenate. Human exposure of arsenic is either through industrial waste or by drinking contaminated water (sources of contamination are pesticides , herbisides,paints and fungisides)(7).The absorbed arsenic gets accumulated in larger concentration in kidney ,heart, liver and lungs in human body whereas it is stored in lower amount in muscles and neurons (8). Aggregation of arsenic (As) in these organs causes many disorders which include diabetes, cancer, hepatotoxicity, cardiac

dysfunction, and neurotoxicity According to **WHO** the permissible limit of arsenic is 10 µg/l and the utmost permitted limit is 50 µg/l of drinking water (9).

Mechanism of toxicity of arsenic:

Arsenic is capable to interact with the sulfhydryl group present in enzymes and proteins and to replace phosphorus (P) in many biochemical reactions (10). Arsenic in-vitro reacts with sulfhydryl (R-SH) groups present in protein to deactivate some of the enzymes such as dihydrolipoyl dehydrogenase and thiolase thereby inhibiting the process of oxidation of pyruvate and betaoxidation of fatty acids (11). Metabolism of arsenic take place by its methylation as well as by reduction processes. Methylation of harmful inorganic compounds of arsenic takes place by microbes like algae, bacteria, fungi as well as by humans to form monomethylarsonic acid (abbreviated as MMA) and dimethylarsinic acid (abbreviated as DMA) (12). Inorganic arsenic species (iAs) through the process of biotransformation are enzymatically converted into methylated arsenicals that are considered to be the final metabolic products and are the biological markers of acute exposure of arsenic,



The process of biomethylation is considered to be the detoxification technique and the end products of the process are found to be methylated inorganic arsenic species (iAs) like monomethylarsonic acid i.e. MMA(V) and dimethylarsinic acid i.e. DMA(V) which are excreted out of body through urine. This is the biological indication of the chronic exposure of arsenic. In the process of excretion the MMA(III) formed in the reaction does not get excreted and it persists inside the human body as intermediate. This MMA(III) is detected to be extremely toxic and is responsible for the arsenic induced carcinogenesis (13).

Mercury

Mercury is present in hair dyes, cosmetics, dental amalgams and lighting. The other source of mercury is coal fired plants and chlor alkali industry. Mercury is found to be one of the exceptionally harmful metal. Mercury is the only metal that exists in liquid state at room temperature. Various oxidation states of mercury include elemental mercury (Hg^0), mercurous (monovalent state Hg^{+1}) and mercuric (divalent state Hg^{+2}). Mercury mainly exists in three forms which include metallic elements (Hg^0), inorganic salts (mercurous and mercuric) and organic compounds (present in three forms: aryl mercury compounds, short chain alkyl compounds and long chain alkyl compounds of mercury) each of which possesses different toxicity and bioavailability. Each and every form of mercury is toxic. The only difference is the way of absorption and biotransformation into the other states. Since mercury easily vaporizes at room temperature, the main route of absorption is often through inhalation to lungs. Human being can be infected with mercury through the anthropogenic activities like mining, waste water discharge, agriculture or industry waste (14). Methylmercury may be neurotoxic compound which is accountable for the destruction of microtubule, damage of mitochondrial, peroxidation of lipids and the accumulation of neurotoxic molecules like glutamate, serotonin and aspartate (15). The main target organ of mercury is brain yet it can damage any body part resulting into the breaking down of muscles, nerves and kidneys as well. It can disrupt the potential of the membrane and may hinder with the intracellular calcium equilibrium. Inorganic mercury salts are found to be nephrotoxic (16). Vapours of mercury can cause acute bronchitis, asthma and temporary respiratory problems. According to **WHO** the levels of mercury in the water should not exceed one microgramme per litre.

Mechanism of toxicity of mercury:

Mercury ions may cause toxicity by precipitation of protein, inhibition of enzyme and their specific corrosive activity. Mercury links to numerous biological structures blocking their activity. It has a high affinity for sulfhydryl groups (-SH) of amino acids, proteins, enzymes, and sulfur-containing antioxidants such as N-acetylcysteine (NAC), α -lipoic acid (ALA), and glutathione (GSH). Glutathione is the most potent intracellular and mitochondrial antioxidant for protecting against oxidative stress, inflammation, and cardiovascular diseases (17). Proteins (including enzymes) with phosphoryl ($-PO_3^{2-}$), carboxyl ($-COOH$), amide ($-CONH_2$), and amine ($-NH_2$) groups are readily available and highly vulnerable to react with mercury compounds. When get bound to mercury, most of the proteins become inactive. Mercury can bind itself to the metalloproteins causing the replacement of zinc (Zn), copper (Cu), and some other trace metals, and becomes competitor for selenium, decreasing the efficacy of the metalloenzymes. The mercury-selenium (Hg-Se) complex formed is responsible for decreasing the accessibility of selenium (Se) for the formation of the enzyme glutathione peroxidase which is responsible for the break down of hydrogen peroxide (H_2O_2) and other toxicants. Elemental mercury vapours are highly soluble in lipid which permits it to cross cell membranes very easily. Elemental mercury can also be easily oxidized to the mercuric state (Hg^{2+}). The divalent mercuric salts are more soluble in comparison to the monovalent mercurous

salts. Therefore the mercuric compounds when ingested gets absorbed at a more rapid rate than mercurous compounds and are responsible for causing greater toxic effect. Just about ten percent of an inorganic salt (whatsoever may be the oxidation state) is consumed in comparison to ninety percent absorption which takes place via the gastrointestinal (GI) track in organic forms. That way the inorganic forms are readily accessible within the gastrointestinal track to apply destructive consequences for the gastrointestinal mucosa. The organomercurial compounds may be present in form of long-chained aryl mercury compounds as well as short-chained alkyl mercury compounds. Out of these two forms the short chained alkyl mercury compounds like methyl mercury causes more hazard. These compounds may be easily and completely absorbed from the gastrointestinal tract and then are diffused to the brain, kidney, liver and other vital organs. Excretion mainly takes place in faeces. Excretion of aryl mercury compounds takes place in the form of mercuric ions.

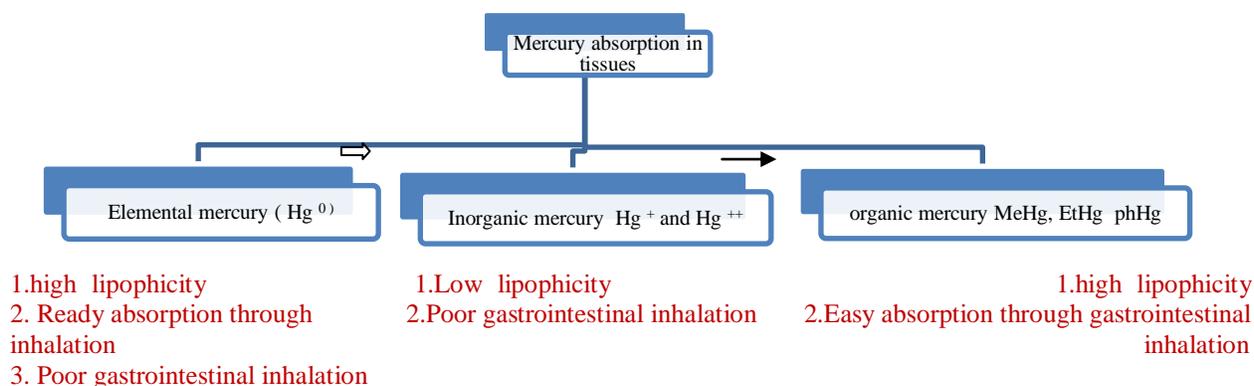


Fig:- Bioavailability and toxic effects of mercury and its compounds. Oxidation in air, and enzymatically in red blood cells and tissues; → Biomethylation by sulfate-reducing bacteria.

Lead

Lead is widely used in paints as a pigment and also to enhance the consistency and durability of paints. Nonbiodegradable nature of lead makes it persistence in the environment for a long time. Lead toxicity results in irreversible health hazards. Human beings are mainly exposed to the lead toxicity through cigarette smoke, drinking water, food they eat, contaminated pollutants of industrial waste and domestic sources. The industrial wellsprings of lead incorporate fuel, house paint, plumbing pipes, lead slugs, faucets, stockpiling batteries, pewter pitchers and toys (18). Lead toxicity affects the central nervous, hematopoietic, hepatic and renal system in the human resulting into serious disorders (19). According to WHO the acceptable limit of lead in water is 10 microgrammes per decilitre ($\mu g/dL$). A person suffers from Chronic toxicity of lead when its level in blood reaches to about 40–60 $\mu g/dL$. Chronic toxicity is indicated by continuous vomiting, dullness in body, deliriousness, convulsions, encephalopathy and coma (20).

Mechanism of toxicity of lead :

One of the significant mechanism by which lead exerts its poisonous impact is through biochemical procedures that incorporate lead's ability to hinder or copy the activities of calcium and to associate with proteins (21). Lead can interfere in the normal functioning of the biological molecules by a number of mechanisms by binding itself to them. Lead can bind itself to the sulfhydryl (SH) group and amide ($CONH_2$) groups of enzymes decreasing their activities by changing their composition and structure. Lead may likewise contend with the cations of essential metals for their binding positions restraining the activity of enzyme or changing the transportation of the cations of essential metals like calcium (22). Living cells suffer from lead toxicity by following the ionic mechanism as well as oxidative stress. Oxidative stress in living cells is chiefly a result of imbalance between the generation of free radicals and formation of antioxidants (under normal circumstance there is a balance between free radical and antioxidants) for the detoxification of the active reaction intermediates or to restore the resulting injury.

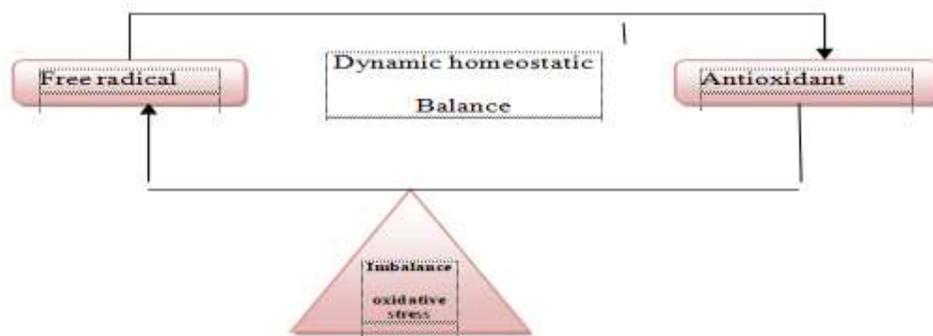


Fig:- Balance Between Free Radicals And Antioxidants Any Deviation From It Can Cause Oxidative Stress Leading To Cell Death.

Antioxidants like glutathione, present in the cell protects it from free radicals such as H_2O_2 , OH^* . The level of ROS (reactive oxygen species) increases and that of antioxidants decreases under the influence of lead (23). As glutathione is present both in reduced glutathione (GSH) and oxidized glutathione disulfide (GSSG) forms, the reduced form of glutathione (GSH) forms its reducing correspondents ($\text{H}^+ + \text{e}^-$) from the thiol (-SH) groups of cysteine to ROS (reactive oxygen species) in order to stabilize them. The reduced form of glutathione (GSH) preferably binds with other molecule of glutathione in presence of enzyme glutathione peroxidase (GPx) and forms glutathione disulfide (GSSG) after donating the electron. The reduced form of glutathione (GSH) represents for ninety percent of the total glutathione content present whereas the oxidized form of glutathione (GSSG) represents for about ten percent under normal circumstances. However under the condition of oxidative stress, the concentration of glutathione disulfide (GSSG) exceeds the concentration of reduced glutathione (GSH). An additional biological marker for the oxidative stress is the peroxidation of lipids because the free radicals accumulate electrons from the molecules of lipid that are present inside the membrane of cell and finally causes the lipid peroxidation (24). Reactive oxygen species (ROS) at a very high concentration may cause the constitutional damage of cells, nucleic acid, proteins, cell membranes and also lipids thereby results in a stressed condition at the cellular status (25).

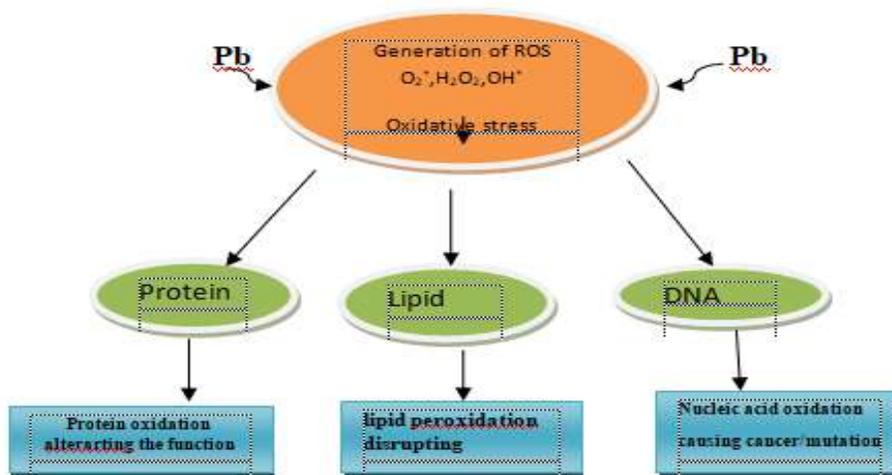


Fig:- Possible mechanism and targets for lead-induced oxidative stress.

Chromium

The heavy metal chromium generally exists in nature in a trivalent form. However certain proportion of hexavalent form is also present. This composition is highly unstable and hence it is a powerful oxidizing agent and therefore can cause serious health effects. Chromium is widely used in chromium steel, fertilizers, electroplating, metallurgy, paints and pigment industry petroleum and paper industry. Various industrial disposals, use of fertilizers as well as anthropogenic activities may release Cr in the atmosphere (26). The metal chromium does not cause air pollution directly but it can transmit the suspended particulate matter (SPM) in the environment. It is observed during the

recent years that hexavalent chromium is the main cause of environmental pollution (27). According to WHO the level of hexavalent chromium in potable water should not be more than 0.05 mg/L.

Mechanism of toxicity of chromium :

The cell membrane permeability of trivalent chromium is low and is less harmful whereas hexavalent chromium is more active to pass through the cell membrane for isoelectric and isostructural anions like SO_4^{2-} and HPO_4^{2-} channels and these chromates are taken up through the process of phagocytosis. Chromium can transform to the mobile hexavalent state if it is strongly heated with a corrosive oxidizing agent like soda ash. Because of the strong oxidizing nature Cr(VI) can be easily reduced to a transitory species of Cr(V) and Cr(IV) both of which are quite different in nature than Cr(III). Cr(V) which is comparatively a long lived species is stabilized by glutathione and consequently the intracellular reduction of Cr(VI) is a process of detoxification when reduction takes place away from the target area. In case the intracellular reduction of Cr(VI) happens near the target area, it might activate Cr. Chemical reactions between Cr(VI) and the biological reducing agents such as ascorbate and thiols leads to the production of reactive oxygen species (ROS) such as hydrogen peroxide (H_2O_2), superoxide ion (O_2^-), and hydroxyl radical ($\cdot\text{OH}$), finally causing oxidative stress in the cell resulting in the damage of deoxyribos nucleic acid (DNA) and proteins (28). hexavalent chromium has been proved to be more deadly than the trivalent form of chromium because the hexavalent chromium can more easily enter inside the cells in comparison to the trivalent chromium and it finally gets reduced to Cr(III). Since the hexavalent chromium can easily cause mutation (mutagenic nature) it has been categorized by the international agency for the research on cancer (IARC) as group 1 carcinogen to humans.

Aluminium

Aluminium is third among the most abundant metals present in earth crust (29). It is imperfectly absorbed following either oral intake or inhalation. In environment Aluminium exists in tripositive (Al^{3+}) oxidation state only. The chief source of aluminium exposure in human are through food additives, beverages, cosmetics, drinking water and medicines containing aluminium such as buffered aspirin (buffered with magnesium carbonate, calcium carbonate and magnesium oxide) and antacids. Aluminium compounds are absorbed at a poor rate in human. Presence of excessive amount of aluminium in the body of a human being is indicated by the common symptoms such as vomiting, skin rashes, nausea, diarrhoea, mouth ulcer, arthritic pain etc. Aluminium binds itself to various ligands present into the blood and is transported to every organ and the highest concentration is in lung tissues and bones. For healthy individuals the aluminium level in bone tissues varies from 5 to 10 mg/kg whereas serum level ranges from 1 to 3 $\mu\text{g/L}$ in healthy person.

Mechanism of toxicity of aluminium:

Interaction between Al and plasma membrane, apoplasmic and symplasmic targets may result in aluminium toxicity (30). Mg^{2+} ion and Fe^{3+} ion are replaced by Al^{3+} ion in human which may result in disturbances associated with intercellular communication, cell growth and secretory functions. The changes that are evoked in neurons by aluminium are similar to the degenerative injuries as seen in Alzheimer patients. Neurotoxicity effects like neuronal degeneration (Neuronal atrophy) in the locus ceruleus (LC), striatum (primarily the dorsal striatum) and substantia nigra (SN) are the complications associated aluminium toxicity (31).

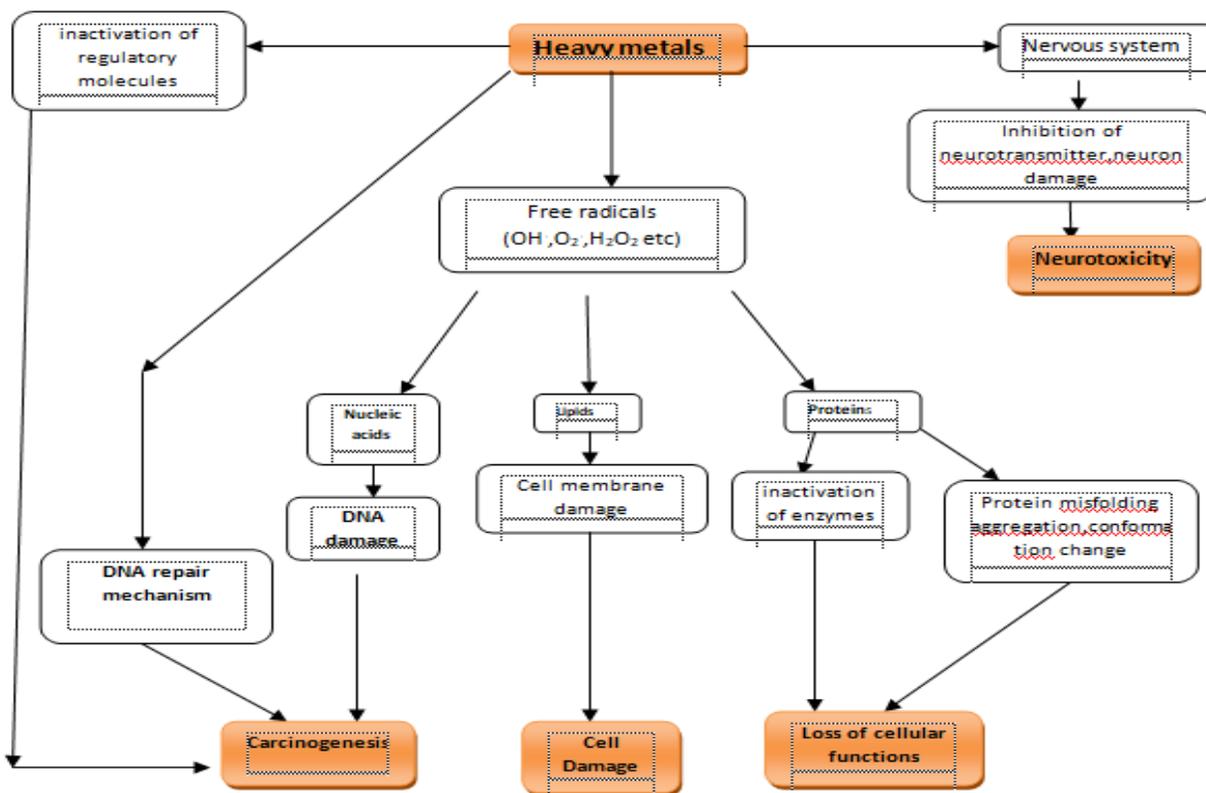


Fig:- Pathway of sources of heavy metals and human exposure.

Some common diseases related to heavy metal exposure

Heavy metals are of common occurrence in our environment and in our diet as well. Many of these are necessary in small amount to maintain a good health and normal functioning of the body. But if these metals accumulate in body in concentration above the required level then these may cause serious damage. The toxicity of metal ions is caused by the chemical reactivity of the ions with enzymes, proteins and cell membrane systems. Accumulation of heavy metals may damage the functioning of vital organs like liver, kidney, lungs and brain. Exposure to these metals for a long duration may lead to progressive muscular and neurological degenerative processes and result into Parkinson's disease, muscular dystrophy and Alzheimer's disease. Some of the metals on long term exposure may result into cancer (32). Accumulation of the heavy metals on some specific organs depends primarily on the route of exposure and chemical state of metal like its volatility, valency and solubility in lipids etc.

Arthritis:

Inflammation of joints is caused by the exposure to certain heavy metals like Fe, Cu, Cd, Pb and Hg for a long time. Osteoarthritis (OA) is a common disease that affects bone and cartilage. The metal responsible for Osteoarthritis is lead (33) whereas Rheumatoid Arthritis (RA) is related to high blood copper levels. Level of Cu in the patient of Rheumatoid Arthritis is found to be higher than those in a healthy person and osteoarthritis patients (34).

Alzheimer's diseases (AD):

Alzheimer's disease is a chronic neurodegenerative disease which diminishes memory as well as thinking capacity slowly and eventually the capability to accomplish the normal functions of daily need and worsens over the period. Heavy metals like Co, Cd, and Cu adjust the gene expression, reduces the activity of proteins, affects signal transduction, generate ROS/RNS, alter cellular proliferations and differentiations and death, damage cells of brain, DNA damage of brain tissues, leading to neurodegenerative diseases like parkinson disease, amyotrophic lateral sclerosis (ALS) and alzheimer disease (35).

Schizophrenia:

Schizophrenia is a disease related to mental disorder which is induced by oxidative stress generated by the decreased level of the antioxidant resistance enzymes like superoxide dismutase, catalase and glutathione peroxidase (36). Some common symptoms of Schizophrenia are irritation and absurdness in behaviour, perturbed and agitated thoughts and oxidative stress which may be due to the change in levels of some trace metals. In case of schizophrenic patients levels of some of the heavy metals like lead, chromium and cadmium is increased whereas level of some trace metals which are necessary nutritionally like Iron and selenium is reduced (37).

Epilepsy:

Epilepsy is one of the most prevalent non communicable neurologic conditions and is the main cause of disability and mortality affecting individuals of all ages (38). The high rate of head injury and of contaminations and infestations of the central nervous system NS like neurocysticercosis, malaria and invasive bacterial contaminations may be imperative causes. Autoimmune neurological disorders induced by mercury can result into epilepsy. One of the major factors responsible for the epilepsy is deficiency and variation in the level of some essential metals like zinc(Zn), calcium(Ca) and magnesium(Mg) etc.

Kidney disease:

The common heavy metals that have toxic effect on renal system are Pb, Hg and Cd (39). About fifty percent of the accumulated Cd is stored in kidneys (40). Exposure to Cd is associated with chronic kidney disease (commonly called CKD) as it causes glomerular damage which results in progressive decline in Glomerular Filtration Rate (GFR means the rate of flow of blood through glomeruli per minute) eventually causing endstage renal failure especially in adults with hypertension or diabetes. If zinc is taken orally it is non-toxic in nature. However, its large quantity may cause dysfunctioning of the system that may result in the diminishing the growth as well as reproduction. The medical symptoms of toxicity of zinc results in kidney failure (41).

Multiple sclerosis:

Overexposure to mercury (Hg) and lead (Pb) ions is proved to be neurotoxic, especially in case of motor neurons (42). From small to medium levels of exposure to lead can result into increased hypersensitivity and can alter cytokine production, which increases risk of inflammation-associated tissue damage (43). Researches have proved that exposure even to a small amount to mercury in genetically sensitive animals stimulate autoimmune disease and results into disturbance in cytokine production.

Arsenocosis:

Arsenocosis may be described as a chronic sickness that results from drinking water with high amount of arsenic present in it for a long duration of time (such as from five years to twenty years) (44). This disease is also known as arsenic poisoning and may result in various detrimental health impacts which include cancer of kidney, gallbladder and lungs, severe skin problems, cancer of skin(45), blood vessel related diseases of legs, high blood pressure and reproductive system disorders.

Parkinsons disease :

This disease is a neurological disorder which increases progressively and severely affects the movement. Common symptoms of Parkinson's signs may include tremor, slow movement, rigid muscles, loss of automatic movement and change in speech. Certain neurons present in brain gets destroyed or break down because of which they stop producing dopamine (a chemical messenger). Decrease in the level of dopamine causes abnormal functioning of brain which results into parkinson's disease. Oxidative stress is one of the major causes of the Parkinson's disease pathogenesis (46). It is found that the oxidative stress generated due to the free iron can lead to damage of neurons and neurotoxicity. Several epidemiological researches have illustrated a connection between parkinson's disease and exposure to heavy metals like mercury (Hg), manganese (Mn), copper (Cu), lead (Pb) iron (Fe), aluminum (Al), thallium (Tl) zinc (Zn) and bismuth(Bi) (47). Professional exposure to the metals like iron, aluminum, and manganese are found to double the risk of parkinson's disease (48).

Conclusion:-

In this article we have reviewed the mechanism and toxic effects caused by the overexposure of some common heavy metals like arsenic, mercury, lead, chromium and aluminium on human being. These metals are naturally present in earth crust mainly as their sulphides and oxides. Due to multiple uses in day to day life they are released in the environment through several anthropogenic activities. Overexposure to these heavy metals may result into some serious health

consequences including neurological disorders, liver and kidney infections, immunological disorders, endocrine disruptions and various types of cancers. Due to the toxic nature and possible bioaccumulation in various body parts, release of these metals by industrial activities should be monitored mandatorily. Some effective strategies are needed at national as well as international level to detect the areas which have a higher level of heavy metal pollution to achieve the target. Some more modern engineering techniques may be used to avoid the occupational exposure of these metals. Failing to manage the exposure of these metals will end in severe health consequences in future.

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