# Subject: ENVIRONMENTAL SCIENCE
## Paper: 304- ENVIRONMENTAL MONITORING & TOXICOLOGY

### Toxicants of Health Hazards
**(Lead, Mercury, Cadmium, Arsenic, Vanadium, Cyanide, Cobalt, Iron)**

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## Introduction:

In our daily life all the matters of the environment are continuously exposed to various metals pollution from different sources (air, water & food). Almost all metals are toxic at high concentration and some are extremely poisonous even at very low concentration. Metals occur naturally in the earth's crust, and their contents in the environment can vary between different regions resulting is spatial variations of background concentrations. The distribution of metals in the environment is governed by the properties of the metal and influences of environmental factors. In the past three decades, agriculture, industry, pharmaceutical industry and science R&D have exposed human and a number of chemicals represented by metals and organic chemicals. The toxicity of metals depends on its route of administration and the chemical compound with which it is bound.

The contamination chain of heavy metals almost always follows a cyclic order: industry, atmosphere, soil, water, foods and human (Fig-1). Aquatic animals are sensitive to heavy metal pollution. Of them, fish is a great biomarker of metal pollution in water. Metals for which there is no nutritional requirement may react with biological system to cause adverse effects. Excessive doses of nutritionally essential metals can also cause adverse effects. Excessive absorption and/or renal insufficiency or biliary obstruction lead to the breakdown of homeostatic mechanisms and to the accumulation of metals in tissue levels to cause toxic effects. The toxic effects of chemical compounds can be classified as either acute (short-term) or chronic (long-term). The effects of chronic poisoning may be very serious and lead to premature death. Effects of a metal can be categorized as doses that cause: (i) no symptoms or detectable effects (ii) stimulatory effects (iii) therapeutic effects (iv) toxic to harmful effects and (v) death. Continuous exposure to small quantities of metals produces cumulative effects that may result in chronic poisoning with metabolic, nutritional, and neurologic symptoms. In larger does, these salts become acutely toxic. The toxicity depends on the physicochemical properties of the salt.

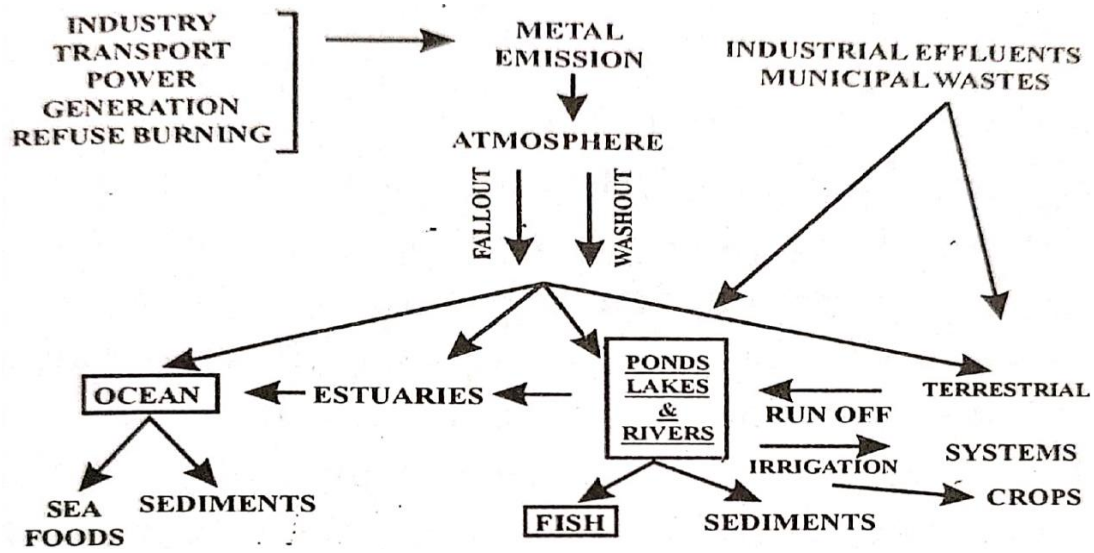



**Figure 1:** Dispersion of Metals in Environment

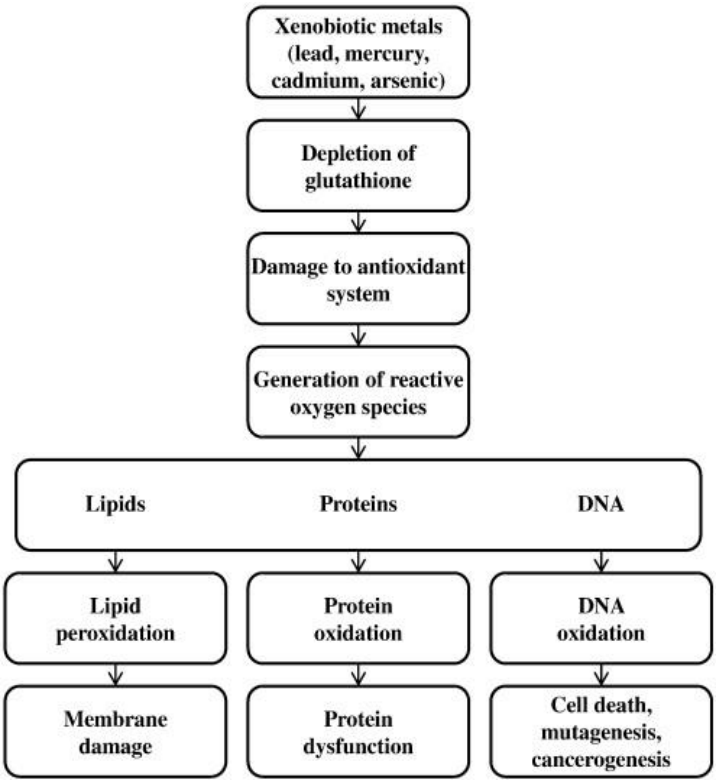



Figure-2 Metal xenobiotics

## 1- LEAD

Lead as a toxicologically relevant element has been brought into the environment by man in extreme amount, despite its low geochemical mobility and has been distributed worldwide. Lead amounts in deep ocean water is about 0.01-0.02 µg/L, but in surface ocean water is about 0.3 µg/L. Lead still has a number of important uses in the present day; from sheets for roofing to screens for X-rays and radioactive emissions. Like many other contaminants, lead is ubiquitous and can be found occurring as metallic lead, inorganic ions and salts. It is principally derived from coal and oil.

Food is one of the major sources of lead exposure; the others are air (mainly lead dust originating from petrol) and drinking water. Plant food may be contaminated with lead through its uptake from ambient air and soil; animals may then ingest the lead contaminated vegetation. In humans, lead ingestion may arise from eating lead contaminated vegetation or animal foods. Lead is deposited in bones as a cumulative poison. It is learnt that most of the lead (Pb) intake by a typical city dweller is from food (200-300 µg/day), air and water (10-15 µg/day). A million tonnes of Pb is deposited into the environment during mining, smelting, winning of metals and from automobiles. The WHO provisional guideline of 0.01 mg/L has been adopted as the standard for drinking water (WHO, 2004). Pb is transported by the blood in the body. It is stored in teeth, bones and soft tissues including the brain.

The toxicity of lead and its compounds are well known and extremely documented. Exposure of man and animals to lead toxicity from the environment, food, water and inhalation of cigarette smoking is increasing. Lead is a cumulative poison that causes both chronic & acute intoxication. Chronic exposure to Pb causes its deposition and immobilization in the bone, from where lead can be mobilized following metabolic disturbances. The G.I. absorption of Pb is increased by low dietary Ca and high dietary vitamin D. The absorption of inhaled Pb salts is rapid and complete. Pb permeates the placental barrier; Pb toxicity is related to the levels of diffusible Pb and its content of soft tissues, not to the content of Pb.

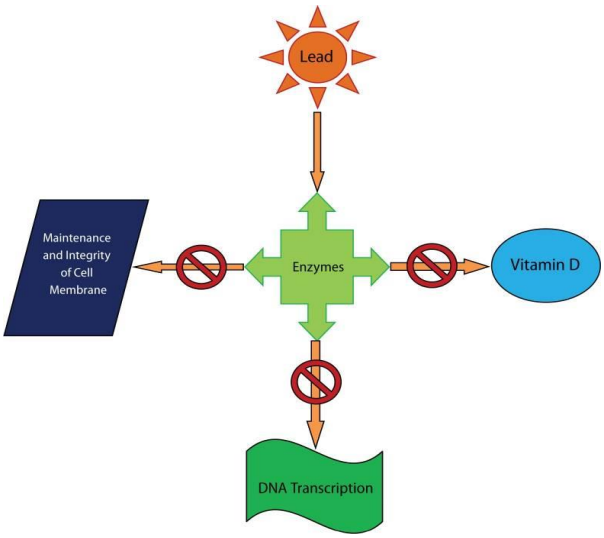



Illustration of the action of lead on enzymes, leading to the disruption of Vit D synthesis, Maintenance of cell membrane and DNA transcription

Acute Pb toxicity symptoms in man are lassitude, vomiting, headache, loss of appetite, loss of memory, uncoordinated body movements, encephalopathy, convulsion, stupor and coma. The other symptoms take a long time to appear as chronic toxicity. They are renal malfunction, anemia, brain and liver damage, joint pain, cancer, hyperactivity and general psychologic impairment.

Lead toxicity in experimental animals includes reduced growth and longevity, impaired renal and reproductive function, splenomegaly, damage to hemo-poietic, central and peripheral nervous system, premature loss of teeth and reduced immune capacity. The detrimental effects in hemopoietic system are abnormal and fragile RBC, impairment in hemoglobin formation by the inhibition of the enzyme delta-ALAD in RBC by lead toxicity. Acute symptom occurs at the blood level of 100–200 μg/dl in adults and 80 –100 μg/dl in children. Chronic symptoms occur at blood level of 50–80 μg/dl. Environmental exposure to Pb has a week but significant effect on the intelligence of children. A study revealed that at the age of 5 or more, a doubling of body lead is associated with a loss of 1-2 IQ points. But below 5 years are not affected.

Signs of chronic lead toxicity appears in adults are tiredness, sleeplessness, irritability, headache, gastrointestinal symptoms etc. The only clinically well-defined symptom associated with the inhibition of haem biosynthesis is anaemia which occurs only at blood lead levels in excess of 40 μg/dl in children and 50 mg/dl in adults. The activity of d-ALAD is a good predictor of exposure at both environmental and industrial levels and inhibition of its activity in children has been noted at a blood lead level as low as 5μg/dl, however, no adverse health effects are associated with its inhibition at this level. Gonadal dysfunction in man, including depressed sperm count has been associated with blood lead levels of 40-50 μg/dl. Reproductive damage may also occur in female occupationally exposed to lead. A study on 700 smelter workers (mean blood level 79.7 μg/L) and battery factory workers (mean blood level 62.7 μg/L) indicated an excess of death from cancer of the digestive and respiratory systems. Lead a poisonous metallic element known to cause several ailments ranging from stomach pain to blindness- is present in the environment because of contamination from lead paints and lead pipes or is emmited into the atmosphere by motor vehicles and industries.

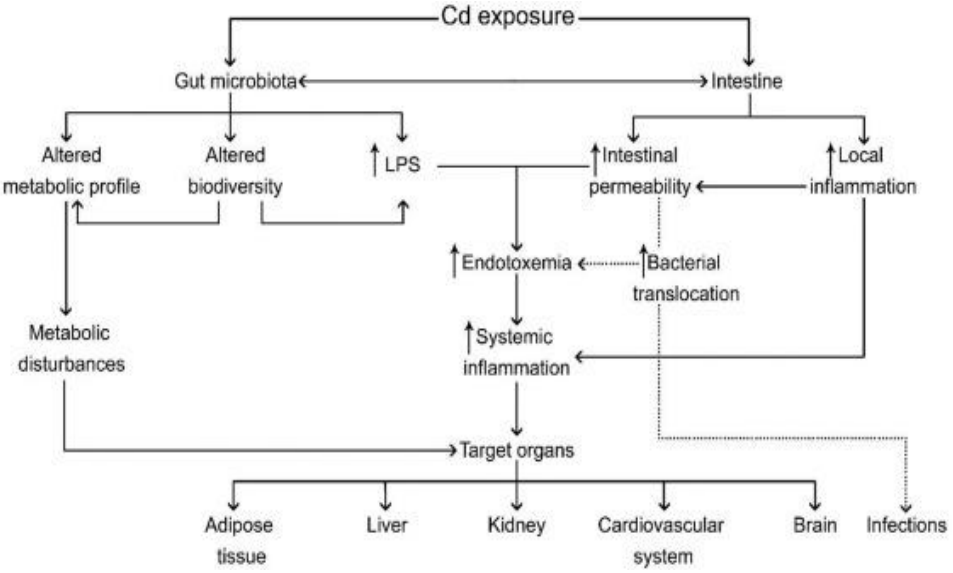
## 2- MERCURY

Mercury is the most toxic heavy metal. It enters the environment as metallic mercury, inorganic mercury compounds and organic mercury compounds through various industris, like pulp and paper industry, chlor-alkali plants, electrical industry, paints, fungicides, moulding processes, batteries and pharmaceuticals. Fossil fuel burning and cement manufacture cause emission of mercury in air. Exposure to high levels of metallic, inorganic, or organic mercury can permanently damage the brain, kidneys, and developing fetus. It causes sensory loss in limbs, impaired vision, loss in hearing and mental retardation. Low and high concentration of mercuric chloride (2 mg/kg body weight and 4 mg/kg body weight respectively) alter the testicular enzyme activity by decreasing several ATPase and by increasing acid and alkali phosphatase in adult albino rats. A single injection of all the concentration of mercuric acetate (5, 10 and 20 × 10–9 mole/g) cause reduction in red blood cell number, hemoglobin content, protein

and nucleic acid content of liver, kidney and spleen of magur fish (*Clarias batrachus L*). A glaring and fatal example of marine pollution through heavy metals was recorded among the residence on the shores of Minamata Bay in 1953 and Niigata Islands in 1965 both in Japan. Both human beings and mammals of this region were serious affected. Methylmercury chloride was identified as the causal toxin, as a byproduct of the manufacture of polyvinyl chloride resin, octanol and dioctol thalate with acetaldehyde as the initial material. Both mercury and methylmercury accumulation occurred in marine organism. The most noted mercury poisoning was the outbreak of "Minamata Disease" in Japanese persons due to consumption of fish as food from the contaminated water. This metal causes headache, diarrhea, blood malfunctioning, defective visions, mental retardation etc. Permissible limits of certain heavy metals in human beings are: Ni -0.2ppm, Pb-01 ppm, As-0.1 ppm, Cd-0.003 ppm, Cr-0.05 ppm, Cu-2.0 ppm, Zn-<5.00 ppm, Hg-0.001 ppm.

### 3- CADMIUM

Cadmium a non essential element, is highly toxic to man and other living biota. Chronic and acute poisoning is reported to occur among the industrial workers. It is naturally present in the environment: in air (0.02 µg/$m^3$), soils (4.5 ppm), and sediments and even in unpolluted sea water. Cadmium is emitted to air by mines, metal smelters and industries using cadmium compounds for alloys, batteries, pigments and in plastics. The outbreak of Cd- poisoning occurred in Toyama city in Japan in the form of itai-itai or ouch-ouch disease. Many people suffered from this disease in which their bones became fragile and muscle contracted along with deformities and pain. Cadmium builds up in the man's body over a prolonged period. Study reports that about 30 mg of Cd of which 33% deposits in kidney, 14% in liver, 3% in pancreas, 2% in lungs and the rest is distributed in the other parts of the body viz., adrenals, prostate, testes and thyroid.




Cadmium toxicity

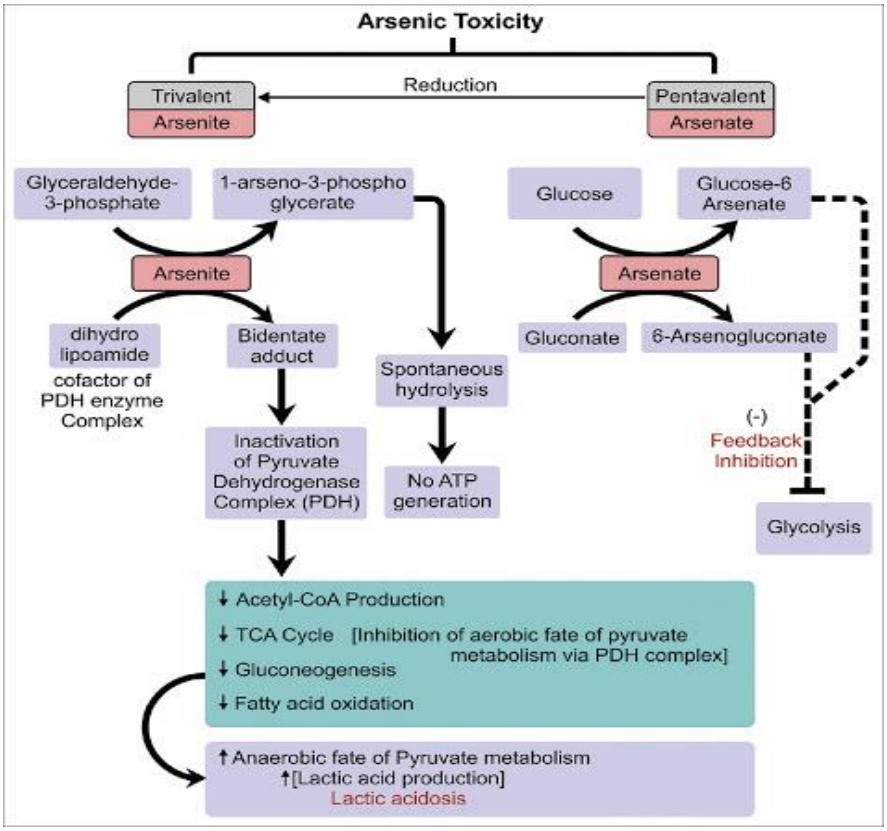
Cadmium has high affinity for sulphur containing legends e.g. –SCH3 or –SH in methionine and cysteine, the amino acids of many proteins. It inhibits certain enzymes like adenosine triphosphate, aldolase, cholinesterase, catalase, succinic dehydogenase etc. Cadmium also activates several such as acid phosphatase, histidine, ammonialyase and phosphorylase of rat liver, cholinesterase of rat brain, heart, spleen, and kidney as well as prolidine carnosinase of swine kidney. Cadmium may cause several chronic diseases in animal and man. Low dose of Cd causes heart disease, hypertension and arteriosclerosis. Mild effects on respiratory organs were found in some groups of industrial workers. Excessive dose of Cadmium also causes reproductive and hepatic damage, pulmonary disorder, anemia, adrenal dysfunction and even prostate cancer. Cadmium cannot create an adverse effect on CNS, so it can not cross the placental barrier.

**4- Arsenic**

Arsenic is generated from fossil fuel burnings. Fertilizer plants liquid effluents contain elemental arsenic ranging from 0.27-3.2 mg/L. its compound had been used as insecticides (Lead arsenate) and herbicides (arsenic trioxide, mono and di sodium arsenate). Arsenic is a deadly poisonous metal. Ingestion as 100 mg caused severe poisoning and more than 130 mg has proved to be fatal. The order toxicity of arsenic compound is- arsines>arsenite>arsenate. Arsenic is mainly present in the liver, lungs, kidneys, blood, bones, teeth and intestinal walls. Female hair contains more arsenic than male. The toxic action of arsines/or arsenite is by attacking –SH groups of an enzyme, thereby inhibiting enxymatic action. The enzyemes producing cellular energy in the kreb's cycle is adversely affected. The inhibitory action has been based on inactivation of pyruvate dehydrogenase by complexation with arsines/or arsenite, whereby generation of ATP is disallowed. Because of its chemical similarity to phosphorus, arsenic is known to interfere with biochemical processes which are involving phosphorus.

The important step in ATP formation involves the enzymatic synthesis of 1,3-diphosphoglycerate from glyceraldehydes 3-phosphate. Arsenic is known to interfere by forming a 1-arseno-3-phospholycerate instead of 1,3- diphosphoglycerate. Phosphorylation gets replaced by arsenolysis which involves hydrolysis to 3-phosphogycerate and arsenate. At higher concentration arsines/or arsenite compounds coagulate proteins probably by attacking sulphur bonds retaining the secondary and tertiary structures of proteins. Thus the main biochemical reactions of As-compounds involve complexation with coenzymes, coagulation of proteins and uncoupling of phosphorylation.

Arsenic gets absorbed through the lungs and skin caused nausea, fainting, salivation, vomiting and burning pain in the stomach. Higher levels of arsenic result in diarrhea, peripheral neuritis, hyperkeratosis and conjunctivitis. Evidence indicates that arsenic in water may be carcinogenic, causing cancer of the skin and liver. It is reported that chronic exposure to arsenic leads to the so-called black-foot disease in certain area.



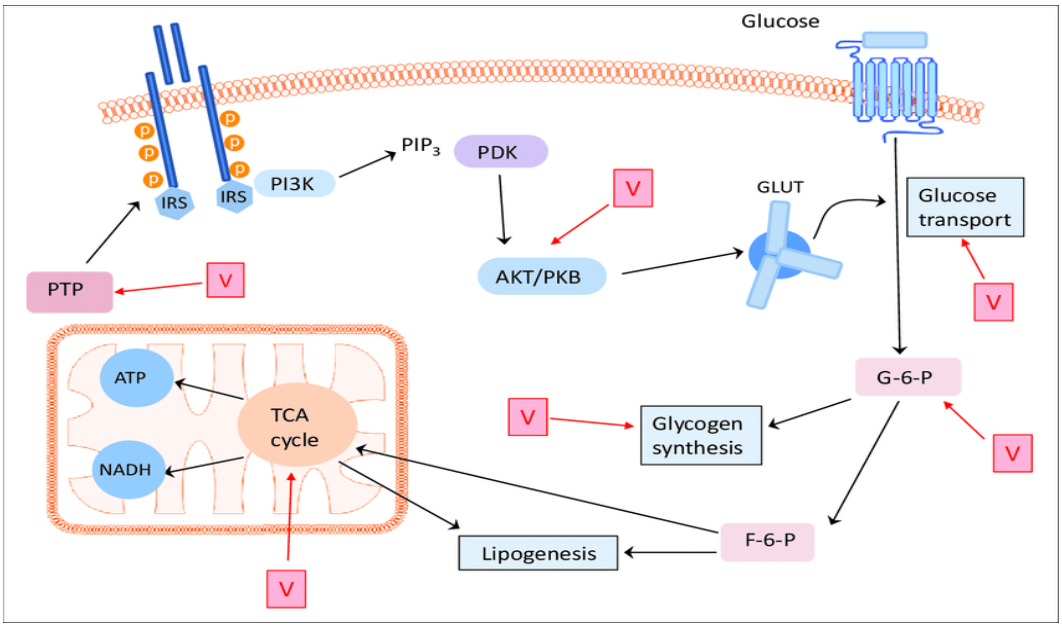

Arsenic effects

## 5. Vanadium

Vanadium is the 22nd most abundant element in the earth's crust with an average concentration of 100 ppm. It exists in oxidation states ranging from 2- to 5+ with 3+, 4+, and 5+ being the most common oxidation states. Vanadium is primarily used in the production of rust-resistant, spring, and high-speed tool steels; vanadium pentoxide is used in ceramics. Vanadium is released to the environment by continental dust, marine aerosols, volcanic emissions, and the combustion of coal and petroleum crude oils. It is naturally released into water and soil as a result of weathering of rock and soil erosion. Ambient air concentrations of vanadium are low, with urban areas having higher concentrations. The general population can be exposed to vanadium primarily through oral (ingestion of vanadium in food) and inhalation routes of exposure. Based on occupational exposure studies, human experimental studies, and studies in laboratory animals, the respiratory tract following inhalation exposure and the gastrointestinal tract, hematological system, and developing organism following oral exposure are the primary targets of toxicity.

Adverse respiratory effects have been reported in humans and animals exposed to vanadium compounds at concentrations much higher than those typically found in the environment. Although the available data in humans are limited, signs of airway irritation (e.g., coughing,

wheezing, sore throat) have been reported in subjects acutely exposed to 0.6 mg vanadium/m3 and in workers exposed to vanadium pentoxide dust.



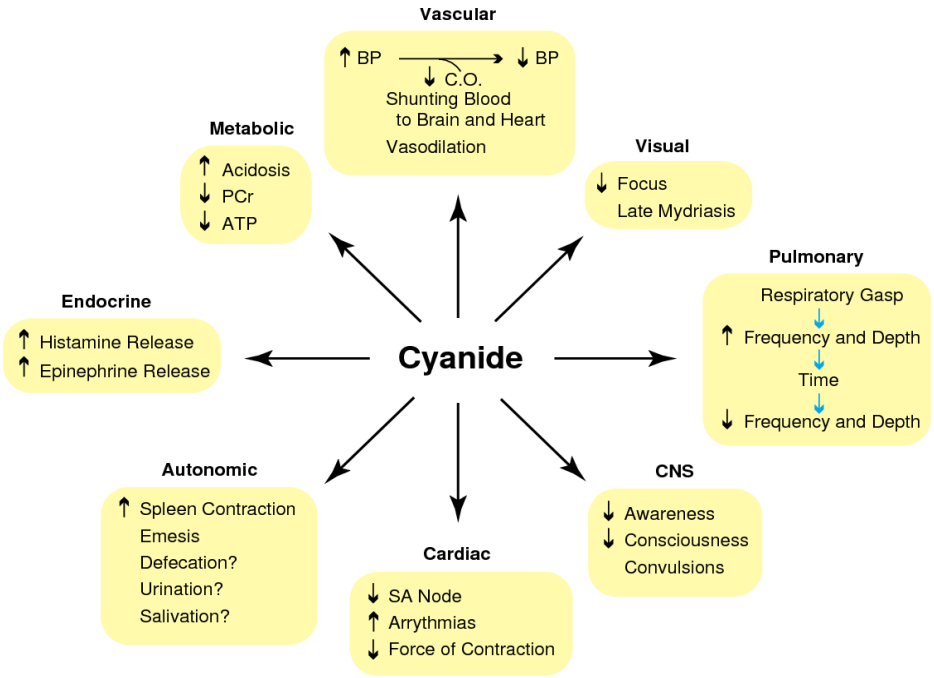

Mechanism of action of Vanadium ions

These effects have persisted for days to weeks after exposure termination and are often not associated with alterations in lung function. Studies in laboratory animals provide strong support that the respiratory tract is the most sensitive target following inhalation exposure to vanadium. A variety of lung lesions including alveolar/bronchiolar hyperplasia, inflammation, and fibrosis have been observed in rats and mice exposed to vanadium pentoxide; the severity of the lesions is related to concentration and duration. The lung effects have been observed following acute exposure to 0.56 mg vanadium/m3 and chronic exposures to 0.28 mg vanadium/m3 and have been observed after 2 days of exposure. Longer duration exposures also result in inflammation and hyperplasia in the larynx and hyperplasia in nasal goblet cells. These histological alterations result in restrictive impairments in lung function; respiratory distress is observed at vanadium pentoxide concentrations of ≥4.5 mg vanadium/m3 . Other sensitive targets of vanadium toxicity include the gastrointestinal system following oral exposure and hematological system following inhalation or oral exposure. Symptoms of gastrointestinal irritation (diarrhea, cramps, nausea) have been observed in humans following bolus administration of sodium metavanadate, vanadyl sulfate, ammonium vanadyl tartrate, or diammonium vanado-tartrate as a treatment in noninsulin-dependent diabetics or patients with ischemic heart disease. The gastrointestinal effects occurred following ingestion of ≥14 mg vanadium and no effects were observed in subjects ingesting capsules containing 7.8 mg vanadium. Diarrhea has also been observed in rats and mice orally exposed to lethal doses of vanadium. Microcytic erythrocytosis (evidenced by decreases in hematocrit, hemoglobin, and mean cell volume and increases in reticulocytes and nucleated erythrocytes) has been observed

in rats exposed to 1.1 mg vanadium/m3 as vanadium pentoxide for at least 4 days. Hematological effects, including decreases in erythrocyte levels, decreases in hemoglobin, and increases in reticulocytes have also been observed in rats orally exposed to 1.18 mg vanadium/kg/day as ammonium metavanadate for 4 weeks. Information on the potential of vanadium to induce developmental effects in humans is limited, but developmental effects have been observed in laboratory animals. Decreases in pup growth have been observed at maternal doses of ≥2.1 mg vanadium/kg/day. At higher doses, decreases in pup survival and gross, skeletal, and visceral malformations and anomalies have been reported; marked decreases in maternal body weight are also observed at these dose levels. An increase in lung carcinoma incidence has been observed in mice chronically exposed to vanadium pentoxide; there is also marginal evidence for lung cancer in male rats (incidence of carcinoma was higher than historical controls but not concurrent controls). Vanadium causes the inhibition of certain enzymes with animals, which has several neurological effects. Next to the neurological effects vanadium can cause breathing disorders, paralyses and negative effects on the liver and kidneys. Laboratory tests with test animals have shown, that vanadium can cause harm to the reproductive system of male animals, and that it accumulates in the female placenta.

**6. Cyanide**

Cyanide is a highly toxic pollutant which enters the environment from many sources. HCN is generally employed as a fumigating agent for destroying rodents in grain bins, buildings and holds of ships. Anthropogenic sources include metal and mineral processing as well as burning polyacrylic. A number of plants such as cassava, clover, and sorghum and seeds of peach, apple, apricot, cherry and plum contain cyanide.




Cyanide Poisoning

Cyanide poisoning is due to its rapid mucous membrane diffusion and penetration, stopping cellular respiration by complexing with ferric ion of cytochrome oxidase and with iron of the heamoglobin forming cyanomethemoglobin. Cyanide is metabolized by three pathways-

a) High concentration of methemoglobin allow minimal formation of cytochrome oxidase cyanide complexes.
b) Rhodonase catalyzes the conversion of cyanide to thiocyanate and
c) A minor pathways combines cystein with cyanide in form 2-amino-thiazolidine-4-carboxylic acid, which is oxidized to carbon dioxide and formate with the gormation of cyanocobalmin.

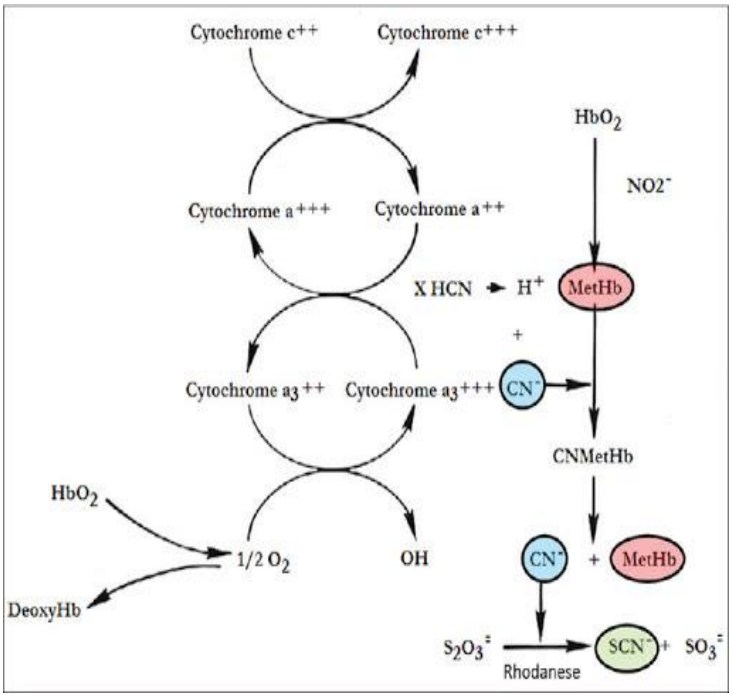



Figure shows metabolized pathways of cyanide

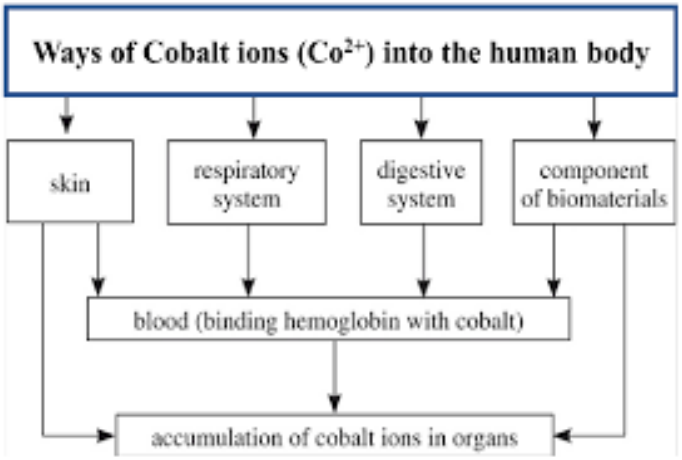
Toxicity of cyanide is exerted by inhibiting oxidative enzymes and intervening the process by which oxygen is used to complete the production of ATP in the mitochondria. Cyanide gets bonded to ferricytochrome oxidase, an iron-containing mettaloprotein (Fe (III)-Oxid) which gets reduced by glucose to ferrous cytochrome oxidase (Fe (II) Oxid). The later can transfer the electrons to oxygen. Cyanide causes hypertension, dyspepsia, vertigo, blood disorder, bone marrow damage, anorexia, vomiting, excitement, depression and death.

**7. Cobalt**

Cobalt attains high concentration factor (CF's) in lower aquatic organism (algae and invertebrates) but it decreases dramatically as the higher trophic levels are reached. Absorption of cobalt by invertebrates via ingestion of food particles, whereas absorption by the vertebrates via gill from the water. The mammals, birds, reptiles etc. have significantly higher cobalt concentrations than other lower organism. Cobalt appears to concentrate more in bone than in

soft tissue. Several studies have reported daily cobalt intake from food. Grains and cereals contain higher concentration of cobalt than potatoes.

The mode of action of cobalt is multilocular. The effect of this metal are produced by enzymatic impairment and this in turn leads to depressed tissue respiration causing depressive effects on energy metabolism. $Co^{2+}$ blocks the krebs citric acid cycle and cellular respiration. Cobaltous chloride inhibits the synthesis of cytochrome P-450. Synergistic effects of cobalt are indicated by cardiomyopathy, polycythemia and thyroid lesions.




The toxicity of cobalt in human appears to be by enzyme inhibition. It causes dyspnea, abdominal pain, nausea, cyanosis, hepatomegaly, massive cardiac enlargement venous distension, peripheral edema, gallop rhythm, tachycardia, hypotension and electrocardiographic changes. Interference of cobalt with cardiac metabolism produces dilation of the heart and secondary thrombosis. Targets of cobalt toxicity in man also include goiters, hypothyroidism, central and peripheral system. Some scientists reported cobalt is a potentially hazardous chemical exhibiting tumor causing properties. A study observed detrimental effects of cobalt in maternal and fetal blood. Cobalt compounds inhibit pregnancy in rats and hamster the fertilized egg before implantation. It also shows teratogenic effect.

**8. Iron**

Iron is chemically active and forms two major series of chemical compounds, the bivalent iron (II), or ferrous, compounds and the trivalent iron (III), or ferric, compounds. Iron is the most used of all the metals, including 95 % of all the metal tonnage produced worldwide. Iron is believed to be the tenth most abundant element in the universe. World production of new iron is over 500 million tonnes a year, and recycled iron add other 300 million tonnes. Economically workable reserves of iron ores exceed 100 billion tonnes. The main mining areas are China, Brazil, Australia, Russia and Ukraine, with sizeable amounts mined in the USA, Canada, Venezuela, Sweeden and India. Iron can be found in animal food, whole meal products, potatoes and vegetables. The human body absorbs iron in animal products than iron in plant products.

Iron is an essential part of heamoglobin; the red colouring agent of the blood that transports oxygen through our bodies. Iron may cause conjunctivitis, choroiditis, and retinitis if it contacts and remains in the tissues. Chronic inhalation of excessive concentrations of iron oxide fumes or dusts may result in development of a benign pneumoconiosis, called siderosis, which is observable as an x-ray change. No physical impairment of lung function has been associated with siderosis. Inhalation of excessive concentrations of iron oxide may enhance the risk of lung cancer development in workers exposed to pulmonary carcinogens. $LD_{50}$ (oral, rat) =30 gm/kg. ($LD_{50}$: Lethal dose 50. Single dose of a substance that causes the death of 50% of an animal population from exposure to the substance by any route other than inhalation. A more common problem for humans is iron deficiency, which leads to anemia.

**OTHER METALS**

**ZINC**

This toxicity occurs from metal welder, zinc containing pesticides etc. Acute and chronic doses of zinc salt can also cause hematological disorder like reduction in RBC and WBC number, Hb content and it can also diminish protein and nucleic acid content of liver, kidney and spleen in experimental animal after accumulation of that metal. Zinc pollution happens kidney problems, pain in leg, fever, vomiting and renal dysfunction, diarrhoea, pancreatitis and pulmonary fibrosis.

**COPPER**

Copper is another toxic heavy metal which also affects blood parameters and tissue proteins and nucleic acids. Copper pollution causes mental disease, coma, anemia, pathological changes in brain tissues, liver and kidney damage, stomach irritation in human being. Copper toxicity can be dispersed from copper pickling and plating, cable factory etc. Acute and chronic treatment with acetate salt of copper (5, 10 and 20 × 10–9 mol/g) cause significant deduction in RBC number, Hb content and PCV. But plasma protein is only reduced with low concentration (5 × 10–9 mol/g) and high concentration of copper (20 × 10–9 mol/g) in a teleost, magur fish. Low, medium and high concentration of copper also diminishes protein, RNA and DNA of liver, kidney and spleen of magur fish. Copper exposure suppresses specific antibody responses and increases evidence of the fish disease. It has been studied with different concentrations of copper as CuSO4 (0.5 and 2.0 ppm). Low dose of copper (0.5 ppm) induce mild oxidative stress with concomitant elevation of GSH (glutathione) and ASA (ascorbic acid) content as antioxidants muscle, kidney, liver, gills of widely consumed freshwater Rohu fish. High concentration of copper (2ppm) leads to severe oxidative stress manifested in the form of LPX and morphoanatomical alteration.

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