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Review Research Paper

Mercury Poisoning: Analytical Aspects with Brief Overview

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Abstract

Mercury (quicksilver) comes under the class of metallic poisons. At room temperature the metal is in liquid form. Although metallic mercury is not poisonous, but it causes poisoning when inhaled in its vapour form, swallowed or rubbed into skin. The toxicity of mercury depends on its chemical form and route of exposure. It affects the immune system, alters genetic and enzyme systems, and damages the nervous system, including incoordination and the tactile, gustatory and visual hallucinations. Clinical features of mercury poisoning along with differential diagnosis have been presented. The pre-hospital, hospital and post-hospital management will help in providing the proper care to the patient along with the treatment which can be done using BAL, DMSA etc. The qualitative as well as quantitative determination of mercury levels can be done with the help of various sophisticated techniques.

Key Words: Mercury, Toxicity, Analysis, Immune system, Nervous system

Introduction:

Mercury is a heavy metal that occurs in several forms, all of which can produce toxic effects in high doses. It is a liquid metal, bright silvery in appearance and is volatile at room temperature. Metallic mercury is not poisonous if swallowed, but in case if it is breathed in a vapour form or applied on skin; it causes poisoning. It occurs in two forms - mercuric and mercurous compounds. Mercuric are soluble and intensely poisonous when compared with mercurous compounds. [1, 2]

Sources & Uses of Mercury:

- Elemental Mercury has been used in thermometers and Sphygmomanometers (Blood pressure measuring apparatus) since long however recently these are being gradually phased out.
- Mercuric chloride is used in electrochemical measurements and in medicine as a purgative and in preservation of anthropological and biological specimens Mercuric oxide is used as a material for cathodes in mercury batteries and skin ointments.
- Mercuric sulphide is used by married Hindu females as vermillion.
- Mercuric cyanide is used in germicidal soaps, photography and cyanogen gas.
- Mercury fulminate is used as a detonator. [2-4]

Mercury Exposure:

- Domestic mercury use such as thermostats, thermometers, batteries etc.
- Dental amalgam
- Consumption of fish and Persons associated with mercury mining. [2- 4]

All forms of mercury can accumulate to some extent. Methyl mercury is absorbed and accumulates to a greater extent than other forms. The levels of methyl mercury increase along the food chain and with age. It can be absorbed quickly by the organism and accumulate in fishes. [2- 4]

Mechanism of Toxicity:

Corrosive sublimate causes coagulation of the albumen of the tissues with which it comes in contact. The result is the immediate destruction of cells. Toxicity depends upon exposure due to:

(a) Elemental mercury
(b) Inorganic mercury compounds
(c) Organic mercury compounds [5,6]

(a) **Elemental Mercury:** such as quicksilver, it is poorly absorbed by ingestion and skin contact. It is hazardous due to its potential to release mercury vapour after heating. Cases of systemic toxicity from accidental swallowing are rare, but in case of attempted suicide via intravenous injection

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may result in systemic toxicity. In humans, 80% of inhaled mercury vapour is absorbed via the respiratory tract where it enters the circulatory system and is distributed throughout the body. Chronic exposure by inhalation, at low concentrations range between 0.7–42 μg/m^3, causes effects such as tremors, impaired cognitive skills, and sleep disturbances.

(b) **Inorganic Mercury Compounds Poisoning:** such as mercuric chloride; it affects the gastro-intestinal tract and kidneys. As they can't enter blood-brain barrier easily, mercury salts inflict neurological damage without continuous or heavy exposure. Mercuric salts are usually more toxic because their solubility in water is greater; thus, they are more readily absorbed from the gastrointestinal tract.

Mercuric cyanide can enter the body via inhalation, ingestion, or passage through the skin. Inhalation of mercuric cyanide irritates the throat and air passages. Heating or contact with acid or acid mist releases toxic mercury and cyanide vapours that can cause bronchitis with cough and phlegm and/or lung tissue irritation.

(c) **Organic Mercury Compounds:** tend to be much more toxic than the element itself and have been implicated in causing brain and liver damage. [7,8]

Onset & Duration:

The symptoms appear in about ten minutes. If taken in large quantity and under favorable conditions death may occur within few hours. In fair proportions death is not due to the immediate effects of poison but due to the secondary effects on the organs. The duration may extend to five or more days. [7]

Normal Levels:

The normal level of mercury in whole blood concentration is < 5μg /L. The normal level of mercury in 24-hour urinary excretion is <50μg/day.

Blood mercury level confirms whether the exposure was recent, because the initial half-life for the elimination of blood mercury is 3 days. Urinary mercury levels indicate the total mercury in body since it is largely excreted by the kidneys.

The half-life of elimination for whole body mercury is 60-90 days. Urinary mercury levels are generally below 10μg/L. According to OSHA (Occupational Safety & Health Administration) exposure limit for workers is 0.01 mg/$m^3$of alkyl mercury over an 8-hours shift. [9, 10]

Table 1: Levels of Mercury in Biological Material

Matrix	Normal Level	Toxic Level
Blood	< 2 μg/L	>3μg/L
Urine	< 10 μg/L	>20μg/L
Nails	< 1 μg/g	>2μg/g

Fatal Dose and Fatal Period:

The acute lethal dose of mercury compounds for an adult is 14–57 mg/kg. The minimum lethal dose of methyl mercury, the organic form of mercury, is 20–60 mg/kg.

The fatal dose of corrosive sublimate is about 1-2 gm. The average fatal dose of mercuric cyanide is 0.6-1.3 gm and that of mercuric nitrate is 4 gm. An intravenous injection of 0.06 gm of metallic mercury proved fatal in case of adult and 20 mg proved fatal in case of child. [7, 8] The usual fatal period is 3-5 days, but death may take place much sooner or later.

Clinical Features/Symptoms:

In case of acute poisoning, the symptoms include an acrid, metallic taste and a feeling of constriction or choking sensation in the throat and difficulty in breathing. Mouth and tongue becomes corroded, swollen and appears greyish-white in colour. Burning sensation in the mouth down to stomach and abdomen, followed by nausea and vomiting. Urine is suppressed or scanty, containing blood and albumin. Pulse becomes quick, small and irregular which lead to circulatory collapse. [9, 10]

In case of chronic poisoning, the symptoms are nausea, digestive disturbances, vomiting and diarrhea. Salivation accompanied by foul breath, swollen and painful salivary glands with inflamed gums. Nephritis may be observed. A brownish blue line may appear at junction of gums and teeth. Brownish reflex formed on the anterior lens of both eyes, which can be seen upon slit-lamp examination. [11, 12]

In addition, different compounds produce specific sign and symptoms of poisoning as under:

(a) Elemental Mercury Poisoning:

- Tremors, Changes in nerve responses, Neuromuscular changes (such as weakness, muscle atrophy, twitching),Disturbances in sensations
- Emotional changes (e.g., mood swings, irritability, nervousness, excessive shyness)
- Insomnia, Headache
- Performance deficits on tests of cognitive function.

(b) Methyl Mercury Poisoning:

- Impairment of the peripheral vision

- Disturbances in sensations ("pins and needles" feelings, usually in the hands, feet, and around the mouth)
- Lack of coordination of movements
- Impairment of speech, hearing, walking and muscle weakness.

(c) Inorganic Mercury:

- Skin rashes, mood swings, memory loss, mental disturbances, muscle weakness.

Diagnosis:

It may be difficult to distinguish between poisoning by amercurial compound and oxalic acid. In case of organic mercury poisoning whole blood or hair analysis is more reliable than urinary mercury levels especially in chronic poisoning. 24-hour collections are more reliable than spot collections. [9]

Laboratory Findings:

1. Blood and urine samples are used to determine recent exposure to elemental and inorganic forms of mercury.
2. Chest x-rays reveals collection of mercury from exposure to elemental mercury or a pulmonary embolism containing mercury. Abdominal x-rays can reveal swallowed mercury as it moves through the gastrointestinal tract.
3. Scalp hair is used in testing for exposure to methyl mercury. Liver and kidney function tests are done for severely exposed persons.
4. Long-term exposure to mercury can be estimated from levels in hair.
5. If large-volume ingestion is suspected, abdominal radiographs should be conducted to detect and follow the transit of mercury in the gastrointestinal tract.
6. Neuropsychiatric testing, nerve conduction studies, and urine assays for N-acetyl-B-D-glucosaminidase and β2-microglobulin have been used to assess delayed and chronic nervous system and renal toxicity. [12]

Analytical Toxicological Methods:

1. Spot Test/Screening:

A. Reinsch Test:

1. About 20 ml of conc. HCl and 100 ml of water is taken in a porcelain basin.
2. Bright copper strip is placed in it with one of the end fixed on the edge of the basin.
3. The solution is boiled for about half an hour to see if the strip, basin and the acid are free from the metal to be tested.
4. If a stain is observed on the strip, then blank experiment is to be carried out again with fresh materials.
5. Suspected material is added to the basin.
6. The solution is again boiled for an hour or more with the addition of water and acid.
7. Shining silvery stain obtained on the copper strip.
8. Shiny silvery stained copper strip is placed in a Reinsch tube and heated slowly.
9. Shining round globules of metallic mercury are observed on the cooler side of tube when viewed under microscope. [13]

B. Micro Test:

1. A portion of the stained copper strip from Reinsch test is taken in a test tube.
2. Few drops of conc. nitric acid are added to it. Solution is evaporated.
3. The residue obtained is taken in dilute hydrochloric acid and spotted on a Silica gel G plate (of thickness 0.2mm).
4. Mercury presence is observed by spraying the chromatogram with dithizone. [14]

C. Test with Diphenylcarbazone:

1. A filter paper impregnated with a freshly prepared 1% alcoholic solution of diphenylcarbazone.
2. A drop of test solution is added to the impregnated filter paper.
3. According to the concentration a violet or blue fleck appears on the filter paper which shows the presence of mercury. [13,15]

D. Test with Cuprous Iodide:

1. One drop of potassium iodide-sodium sulfite solution is taken on a filter paper.
2. A drop of copper sulphate solution is added to it.
3. A drop of test solution is added with the help of a capillary.
4. According to the concentration Red or orange colour is observed which shows the presence of mercury. [15]

E. Test with Stannous Chloride and Aniline:

1. A drop of test solution is taken on filter paper.
2. Few drops of freshly prepared stannous chloride solution followed by a drop of aniline are added to it.
3. A black to brown colour is observed which shows the presence of mercury. [15]

2. Quantitative Analysis:

Quantitative estimation of Mercury can be done by using specific methods of different sophisticated techniques viz. Spectroscopy, Voltammetry & Polarography, Chromatography & Neutron Activation Analysis.

A. Spectroscopy:

Spectroscopy is the interaction between radiation and matter. The methods employed in spectroscopy are based on the measurement of

amount of radiation absorbed or produced by molecular or atomic species of matter.

The spectroscopic methods can be classified according to the involvement of the region of electromagnetic spectrum. [16]

Quantitative determination of mercury can be done by using various instrumentation technique involving spectrometry viz. Atomic Absorption Spectrometry, Inductively coupled plasma- atomic emission spectrometry, Inductively coupled plasma-optical emission spectrometry, Inductively coupled plasma– Mass spectrometry, UV-Visible Spectrometry, Energy Dispersive X- Ray Fluorescence Spectrometry. [13, 17-20]

B. Voltammetry & Polarography:

In an electrochemical cell a time dependent potential is applied and the current flowing as a function of that potential through the cell is measured. In Voltammetry the applied potential produces a change in the concentration of an electro active species at the electrode surface by reducing or oxidizing it. Mercury can be determined by an instrument Trace Metal analyzer using the above technique. [21, 22]

C. Chromatography:

Chromatography is separation technique for molecular mixtures wherein separation is achieved by relative affinity or interaction of solutes with stationary phase (adsorbent), mobile phase and equilibrium attained thereof. Mercury can be analyzed by using Ion Chromatograph coupled with multidimensional detectors achieving high sensitivity and selectivity. [23]

D. Neutron Activation Analysis:

In this technique the sample is bombarded with neutrons, which generates a range of radio isotopes and as these radioisotopes decay they emit radiation which can be measured using β -ve or gamma –ve counters, which is a characteristic for a particular element. Neutron activation analysis is very sensitive and can be used to measure several elements simultaneously but it is very expensive and an access to an atomic reactor is required hence it is used very rarely. [24] In India this facility is also available at Bhabha Atomic Research Centre, Mumbai.

Pre-Hospital Management:

Victims exposed to mercury vapour do not pose for secondary contamination risks to surroundings. Victims whose skin or clothing is visibly contaminated with liquid mercury can contaminate rescuers' equipment, clothing, or the indoor environment. Contamination of clothing or equipment can result in subsequent chronic inhalation hazard to others as the elemental liquid mercury off-gasses.

- **Respiratory Protection:** Positive-pressure, self-contained breathing apparatus is used in situations that involve exposure to potentially unsafe levels of elemental mercury.
- **Skin Protection:** No special clothing is needed unless mercury vapour is being heated; in that case chemical protective clothing is recommended to avoid contamination. Gloves and foot protection are recommended as mercury spreads under nails. Any clothing that comes in contact with liquid mercury should be properly decontaminated or disposed of to prevent further exposure.
- **Eye exposure:** Eyes should be washed immediately with large amount of water by lifting lower and upper lids. Contact lenses should not be worn while handling mercury and its compounds.

Hospital Management:

- **Basic Decontamination:**

Victims who are able to move may assist in their own decontamination. Contaminated clothing and all personal belongings of the individual should be removed and kept in double bag. Exposed skin and hair should be washed with mild soap and water.

Caution should be taken to avoid hypothermia when decontaminating in case of children &elderly. Exposed or irritated eyes should be flushed with plain water or saline for at least 5 minutes. Contact lenses should be removed carefully without causing additional trauma to the eye. If pain or injury is evident, irrigation should be continued while transferring the patient to the Support Zone.

Elemental mercury is not readily absorbed from the gastrointestinal tract and generally does not produce acute toxicity, it will be excreted out through faeces hence emesis is not advised.

- **Transfer to Support Zone:** As soon as basic decontamination is completed, the victim should be transferred to the Support Zone.
- **Support Zone:** Victims who have undergone decontamination or have been exposed only to vapour pose no serious risks of secondary contamination. In such cases, Support Zone personnel require no specialized treatment.
- **Skin Exposure:** Elemental mercury does not cause a chemical burn. Washing the exposed skin with soap and water should

remove any residual liquid mercury if present.

- **Eye Exposure:** Adequate eye irrigation must be ensured. Eyes should be examined for conjunctiva or corneal damage. Patients should be referred to an ophthalmologist in case of apparent or suspected corneal injury.
- **Ingestion Exposure:** Emesis may not be induced and activated charcoal should not be given since elemental mercury is not usually absorbed from the gastrointestinal tract and does not produce acute toxicity.

However, if an individual with gastrointestinal perforation ingests an extremely large amount, mercury might be retained for a long period in the GI tract and decontamination should be considered. [25]

Treatment:

Patient should be approached cautiously for stomach wash with warm water along with magnesium carbonate. Albumin in any form or vegetable gluten mixed with skimmed milk can be used.

Demulcent drinks may be administered for the protection of stomach wall.3-4 tablespoons of activated charcoal should be administered along with 20 gm of magnesium sulphate which hastens the removal of ingested poison. The standard dosage of BAL for inorganic mercury poisoning is 3 mg/kg IM every 4 hours for 2 days, and every 12 hours thereafter for 7 to 10 days or until 24-hour urinary excretion levels are less than 50 µg/L.

Dimercaprol must not be administered in patients with glucose-6-phosphate dehydrogenase deficiency, because it can produce haemolysis. Oral agents such as 2, 3-dimercaptosuccinic acid (DMSA) used as alternatives when dimercaprol toxicity or intolerance develops. Penicillamine is useful as an antidote in the dose of 250 mg to 2 g each day. In children dose is 20 mg/kg body weight.

Hemodialysis is used in severe cases of toxicity when renal function has declined. The ability of regular hemodialysis to filter out mercury is limited because the mode of distribution is through erythrocytes and plasma.

However, hemodialysis, with L-cysteine compound as a chelator, has been found successful. Neostigmine may help motor function in methyl-mercury toxicity. This toxicity often leads to acetylcholine deficiency.

Polythiol is a non-absorbable resin that can help in facilitating the removal of methyl-mercury, which is then excreted in the bile after enterohepatic circulation. Gastric lavage with 5% solution of sodium formaldehyde sulphoxylate reduces mercury chloride to metallic mercury. Egg-whites, milk or animal charcoal can be used to precipitate mercury. High colonic lavage with 1:1000 solution of sulphoxylate twice daily is also effective. [7, 8, 10]

Some Case Reports:

A. Case 1:

A 7 yrs old was referred to hospital for pain in his legs, neck and abdomen for a period of 2.5 months and experienced pain in his extremities for 20 days. The patient had no fever, vomiting or diarrhea, but had reduced appetite and had lost 2-3 kg weight. He had a history of measles and charcoal poisoning.

Body weight was 26 kg and height was 128 cm. The general condition was moderate. On examination other systems were found to be normal. Laboratory test results included routine urinary and blood studies, liver and renal function tests which were normal.

Creatine kinase: 71 IU/L, lactate dehydrogenase: 316 IU/L, antistreptococcal antibody (ASO): 57 TU, C-reactive protein (CRP): <3 mg/dL, ANA: negative; antiDNA: negative, C3: 1.14, agglutination test: negative, Gruber-Widal agglutination test: negative, thyroid function tests were within the normal limits. The patient's history showed the chronic mercury intoxication due to clinical features and high mercury levels in blood sample.

Therapy with D-Penicillamine was started. In the second month of the therapy, abdominal pain was diminished and the patient's extremity pain was also reduced. The patient showed no complaints and therefore his blood mercury levels were assessed together with 2 months intervals. After receiving D-Penicillamine for a period of 8 months, the patient showed no symptoms. [20]

B. Case 2:

The 13-year-old patient was diagnosed with **chronic mercury intoxication.** He came with complained of abdominal pain, extremity pain, and dermal eruptions.

The patient's blood mercury level was 13.8ug/dL. Body weight of patient was 50.5 kg and height 154 cms, blood lead level: 2.20ug/dL, blood mercury level: 12.8ug/dL.

D-Penicillamine therapy was started. Naproxen and carbamazepine was also administered in order to reduce the diffuse body pain. Due to increase in the liver enzyme levels accompanied with proteinuria, D-Penicillamine therapy was stopped and replaced with dimercaprol for a period of 10 days. After liver and renal function tests turned out to be normal;

D-Penicillamine therapy was restarted. 3 weeks after the patient was discharged from the hospital, pain in the extremities and head was reduced and abdominal pain was eliminated. In the second month of therapy, all the symptoms eliminated. The patient received D-penicillamine for a total of 7 months, and then the blood mercury level was carefully monitored during bi-monthly controls for a period of 12 months. [26]

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