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CURRENT APPROACHES IN THE MANAGEMENT OF MERCURY TOXICITY

[1*]Dr. Jagdish Kumar Anant and [2]Dr. S. R. Inchulkar

[1]P.G. Scholar, [2]Professor & HOD, P.G. Department of Agad Tantra Evum Vidhi Vaidyak, Govt. Ayurvedic College, Raipur, Chhattisgarh, India.

***Corresponding Author: Dr. Jagdish Kumar**

P.G. Scholar, P.G. Department of Agad Tantra Evum Vidhi Vaidyak, Govt. Ayurvedic College, Raipur, Chhattisgarh, India.

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ABSTRACT

Mercury poisoning cases have been reported in many parts of the world, resulting in many deaths every year. Mercury compounds are classified in different chemical types such as elemental, inorganic and organic forms. Long term exposure to mercury compounds from different sources e.g. water, food, soil and air lead to toxic effects on cardiovascular, pulmonary, urinary, gastrointestinal, neurological systems and skin. Mercury level can be measured in plasma, urine, feces and hair samples. Urinary concentration is a good indicator of poisoning of elemental and inorganic mercury, but organic mercury (e.g. methyl mercury) can be detected easily in feces. Gold nanoparticles (AuNPs) are a rapid, cheap and sensitive method for detection of thymine bound mercuric ions. Silver nanoparticles are used as a sensitive detector of low concentration Hg^{++} ions in homogeneous aqueous solutions. Besides supportive therapy, British anti lewisite, dimercaprol (BAL), 2, 3-dimercaptosuccinic acid (DMSA. succimer) and dimercaptopropanesulfoxid acid (DMPS) are currently used as chelating agents in mercury poisoning. Natural biologic scavengers such as algae, azolla and other aquatic plants possess the ability to uptake mercury traces from the environment.

KEYWORDS: Quick silver, Mercury compounds, Acute & chronic poisoning, Minamata disease, Chelating agents, Medicolegal aspects, etc.

INTRODUCTION

Mercury (Hg) atomic number 80, is a liquid metal at room temperature and pressure. Mercury freezes at -38.9°C and boils at 357°C. It is sometimes called quick silver and is easily alloyed with many other metals, such as gold, silver and tin.[1] It exists in the environment in three forms: elemental mercury (poisonous as vapor), organic mercury (methyl mercury and ethyl mercury) and inorganic mercury (mercuric mercury) and all these forms have toxic health effects.[2] In recent years, due to abundant availability of various chemicals, the rate of intoxication has been surprisingly increased.[3] People can overuse or misuse drugs, chemicals, and may get poisoned intentionally or accidentally. Similarly, heavy metals, either released from natural sources or from industries wastes pose a consistent health threat to human being.[4] Mercury could be found in different commercial forms. Mercury and its related compounds are being circulated and concentrated in soil and distributed into the air via coal fuels, industrial furnaces or active volcanoes. It then returns to the soil, water, or living organisms. Recycling from atmospheric emission, deposition in water reservoirs and exposure and bioaccumulation in animals and humans is a known example of mercury cycle in the environment.[5]

TOXIC SALTS OF MERCURY[6]

A. Inorganic salts

1. **Mercuric chloride** (corrosive sublimate): Colorless, odorless, prismatic crystals or white crystalline powder, but has a nauseous metallic taste **(Fig.-1)**. It is the most toxic inorganic salt, and commonly the cause of acute poisoning.
2. **Mercurous chloride** (calomel): Heavy, amorphous, white and tasteless powder.
3. **Mercuric sulfide** (cinnabar or vermilion): It is not absorbed through skin, and is as such nonpoisonous (red crystalline powder) **(Fig.-2)**.
4. **Mercuric cyanide, oxide** and **iodide** (scarlet red powder).

B. Organic salts

Include methyl mercury (most toxic), dimethyl mercury, ethyl mercury and phenyl mercury.

Figure-1
Mercuric chloride

Figure-2
Mercuric sulfide

USES[7]

- **Medicine:** Disinfectant, dental amalgam, purgative and diuretic, and earlier used in the treatment of syphilis. A controversial source of organic mercury exposure is thimerosal, a preservative used in vaccines (DTP and hepatitis B) to prevent bacterial contamination.
- **Industry:** Manufacture of thermometer, barometer, calibration instruments, fluorescent and mercury vapor.
- **Miscellaneous:** Electroplating, photography, insecticide, germicide, fingerprint powder, paints and embalming fluid.

MECHANISM OF ACTION[8]

Mercury binds with sulphydryl (SH) groups resulting in enzyme inhibition and pathological alteration of cellular membranes. Elemental mercury and methyl mercury are toxic to the CNS. Metallic mercury vapor is also a pulmonary irritant. Inorganic mercury salts are corrosive to the skin, eyes and GIT, and nephrotoxic. Inorganic and organic forms may cause contact dermatitis.

TOXICOKINETICS[9]

1. **Absorption:** Mercury is absorbed through the GIT and respiratory tract.
2. **Distribution:** After absorption, mercury gets deposited in all tissues, particularly in the liver, kidneys, spleen and bones. When inhaled, the maximum concentration occurs in the brain.
3. **Elimination:** Mainly excreted through the kidneys (urine), liver (bile) and colonic mucous membrane (feces). It passes rapidly to the fetus through placental circulation.

CLINICAL FEATURES[10, 11, 12]

1. **Acute Poisoning:** The three types of mercury have different manifestations:

   I. Elemental (metallic) mercury: As a vapor, it is rapidly absorbed through the lungs, reaching the blood and entering the brain. The clinical picture can be divided into three phases-initial phase manifests itself as metal fume fever, intermediate phase in which severe multi-organ symptoms are seen, and late phase when only CNS symptoms persist.

- **Inhalation** causes headache, nausea, cough, chest pain, bronchitis, chemical pneumonitis, pulmonary edema, gingivostomatitis, fine tremor punctuated by coarse shaking, and CNS symptoms like insomnia, ataxia, restriction of visual field, paresis, delirium and polyneuropathy.
- **Subcutaneous** nodules or granulomas are seen, if injected.

II. Ingestion of inorganic mercuric salts produces extensive precipitation of intestinal mucosal proteins and mucosal necrosis causing bloody diarrhea and shock. If the patient survives, acute renal failure may follow.

III. Organic mercury: Acute exposures tend to have a latency period of one or more weeks. Symptoms typically involve the CNS such as: visual field constriction, ataxia, paresthesias, hearing loss, dysarthria, tremor, neurobehavioral impairment, paralysis and death.

S.N.		Elemental mercury	Inorganic salts	Organic salts
01	Route of exposure	Inhalation (vapors)	Ingestion	Ingestion
02	Primary effect on	Brain, kidney	Blood, kidney, brain	Brain, kidney, liver, blood, hair
03	Respiratory distress	++++	-	-
04	Tremors	++	++	++
05	Ataxia, paresthesia	-	-	++
06	Disturbances of vision and speech	-	-	++
07	Gastrointestinal disturbances	+	++++ (corrosive)	+
08	Kidney injury	+	+++ (glomerular & tubular damage)	+
09	Acrodynia, erethism	+	++	-
10	Chelation with	BAL, DMSA	BAL, DMSA	DMSA

1. Chronic Poisoning (Hydrargyrism)

Chronic poisoning results from.

- Continuous accidental absorption by workers.
- Excessive therapeutic use.
- Recovery from a large dose.
- If an ointment is used as an external application for a long time.
- In the US, exposure to organic mercury is primarily through ingestion of contaminated fish (seafood).

Signs and Symptoms

- Chronic intoxication from inhalation of mercury vapor produces a triad of tremors, neuropsychiatric disturbances and gingivostomatitis.
- Chronic poisoning with inorganic mercury compounds is characterized by non-specific early symptoms such as anorexia, insomnia, abnormal sweating, headache, lassitude, increased excitability, tremor, gingivitis, hypersalivation, loosening of teeth with blue line in the gum, jaundice, increased urination, personality changes, and memory and intellectual deterioration. Glomerular and tubular damage may occur in chronic exposure.
- Exposure to organic mercuric compounds is characterized by paresthesia of lips, hands and feet, ataxia, tremor, dysarthria, constriction of visual fields, deafness, and impairment of motor speed, memory and coordination.

SPECIFIC FEATURES/DISEASES[13, 14]

1. **Minamata disease:** In Minamata Bay (Japan), a factory discharged inorganic mercury into the water. The mercury was methylated by bacteria and subsequently ingested by fish. Local villagers ate the fish and began to exhibit signs of chronic mercury poisoning. **Minamata disease** is due to chronic organic mercury intoxication caused by eating contaminated fish and shellfish. Symptoms include disturbances in hand coordination, gait and speech, chewing and swallowing difficulties, visual blurring, tremors, rigidity, seizures and clouding of consciousness.
2. **Acrodynia or Pink disease:** It is seen mostly in children due to idiosyncratic hypersensitivity reaction to repeated ingestion or contact with mercury (allergic reaction to inorganic mercury). **Signs and symptoms:** There is pinkish morbilliform/ acral rashes, desquamation of palms and soles, pain in the extremities, flushing, itching, swelling, tachycardia, hypertension, excessive salivation or perspiration, weakness, irritability, photophobia, anorexia, insomnia, and constipation or diarrhea.
3. **Hatter's shake:** In the UK, during 18–19th century, mad hatter syndrome was seen due to occupational exposure of mercury among people making felt hats. They developed neurotoxic effects including tremor, and shyness and irritability characteristic of erethism.
4. **Mercurialentis:** It is a peculiar eye change due to exposure to mercury vapor. It is due to brownish deposit of mercury through the cornea on the anterior lens capsule. Slit-lamp examination gives a malt-brown reflex from the anterior lens capsule. It is bilateral and has no effect on visual acuity.
5. **Mercurial erethism:** Erethism is seen in the chronic phase of the inorganic mercury toxicity. This cluster of symptoms was first described by Kussmahl in persons working with mercury in mirror manufacturing firms, and the term is used to refer to the neuropsychiatric effects of mercury toxicity. These include: Insomnia, Depression, Anxiety, Amnesia, Timidity and shyness, Frequent blushing, Explosive irritability, Loss of confidence, Feeling of embarrassment, Suicidal melancholia, Emotional instability, e.g. sudden attacks of anger, Delusions and Hallucinations.
6. **Intention tremors (Danbury tremors/shaking palsy):** It occurs first in the hands, then progresses to the lips and tongue, and finally involves the arms and legs. Tremor is moderately coarse and is interspersed by jerky movements. The patient may not display much tremor during an accustomed job, but if he is being observed, he may begin to shake violently. In the advanced stage, the person is unable to dress himself, write legibly or walk properly. They are also called **hatter's shakes or glass blower's shakes**, as they are common in persons working with mercury in glass-blowing and hat industries. The most severe form of tremors is known as **concussion mercurilis**.

FATAL DOSE[15, 16]

- Metallic mercury (I/V): 0.06 gm.
- Mercuric chloride (oral): 1-4 gm.
- Mercuric cyanide (oral): 0.6-1.3 gm.
- Oxide of mercury (oral): 2 gm.
- Methyl mercury: 10-60 mg/kg of body weight.
- Mercury vapor: 10 mg/m^3.

FATAL PERIOD[17, 18]

- 3–5 days.

LABORATORY DIAGNOSIS[19, 20, 21]

Acute mercury poisoning can be detected by measuring blood levels, whereas urine and hair analysis help confirming chronic exposure.

- The DMPS provoked urine challenge test is sometimes performed for chronic exposure.
- Blood mercury level > 10 µg/dl, and 24 hours (h) urinary excretion of mercury > 20 µg/l indicates toxicity. A hair mercury level > 5 ppm indicates chronic toxicity.
- Urine and blood mercury levels are assessed by atomic absorption spectrophotometer. Mercury concentration of hair is best assessed by neutron activation analysis.
- X-ray

MANAGEMENT[22, 23, 24]

- In case of *inhalation*, the victim is immediately removed from source of exposure and supplemental oxygen is given, and observed for the development of acute pneumonitis and pulmonary edema.
- Egg whites, milk or animal charcoal to precipitate mercury. Emesis is not induced because of the risk of serious corrosive injury.
- Gastric lavage with 250 ml of 5% sodium formaldehyde sulfoxylate. About 100 ml of this solution is left in the stomach. Lavage can be done with egg-white solution or 2–5% solution of sodium bicarbonate.
- Polythiol resins helps in binding mercury in the GIT.
- High colonic lavage with 1:1000 solution of sulphoxylate twice daily. Whole bowel irrigation may be done.
- BAL is the traditional chelator of choice (10% solution in oil, 3–5 mg/kg IM every 4 h for 2 days, tapered to 6 hourly for 1 day and then 12 hourly for 7 days), but oral agents are preferable.
- **DMSA or succimer** (10 mg/kg orally every 8 h for 5 days and then 12 hourly for 2 weeks) is a good oral chelator with increased mercury excretion.
- D-penicillamine is an alternative oral treatment, but it may be associated with more side-effects and less efficient Hg excretion.
- There is no role of for dialysis, hemoperfusion or repeat dose charcoal in removing metallic mercury or inorganic salts. However, hemodialysis/ peritoneal dialysis may be required in case of renal failure.
- Maintain electrolyte and fluid balance.
- Symptomatic treatment.

POSTMORTEM FINDINGS [25, 26]

- Body looks emaciated.
- **GIT:** Mucosa shows inflammation, congestion and grayish corrosion. Ulceration or even gangrene of large intestine may be seen.
- **Kidneys:** Acute proximal tubular damage and glomerular degeneration or glomerular nephritis (membranous glomerulopathy) may be seen.
- **Liver:** Congested and shows cloudy swelling or fatty change.
- **Heart:** Fatty degeneration and subendocardial hemorrhage.

MEDICOLEGAL ASPECTS [27, 28]

A. Suicidal and homicidal poisoning is rare. However, cases of deliberate intravenous or subcutaneous metallic mercury injection have been reported.

B. Accidental poisoning may occur from.

- Accidental ingestion may occur from broken thermometers.
- Accidental ingestion of antiseptic solutions containing mercuric chloride/cyanide.
- Soluble salts employed as vaginal douches.
- Absorption of mercurial preparations applied to the skin.
- Intravenous administration of organic mercurials, such as diuretics.
- In children, swallowing the sulfocyanide of mercury tablet, the constituent of Pharaoh's serpents, or elemental mercury because of its bright gray appearance.

CONCLUSION

Mercury exposure leads to harmful effects on almost every organ and system. It should be considered as a silent threat to environment and human life, through the world. The main concern is with the more subtle effects arising from prenatal to adult's period and exist delay development and cognitive changes in children and clinical manifestations in adults. New protocols for the treatment of poisoning such as access to new antidotes, chelating agents, combination therapy of different chelating agents and specific nanosorbents can help in the management of mercury poisoning. There are risks of mercury compounds for health in the worldwide. Therefore governmental and non-governmental organizations need to identify highly prone people to mercury exposure, and make sure safe food and drinking water. In addition, it is necessary to pay attention to the safe transport and handling of mercury compounds.

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