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Review Article

MERCURY POISONING AND MANAGEMENT: A SYSTEMATIC REVIEW

JEMBULINGAM SABARATHINAM*, VISHNU PRIYA V, GAYATHRI R

Department of Biochemistry, Saveetha Dental College, Chennai - 600 077, Tamil Nadu, India. Email: drjembu@gmail.com

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ABSTRACT

A great number of literatures have been documented the destructive effects of the heavy metal toxin on the brain, kidneys, and nervous systems. Mercury is one of such chemicals of the environmental toxin which produces adverse effects causing mercury poisoning a leads to accumulation in the tissues of the body. Mercury occurs in various forms even though they are interchangeable which is the deadly feature of this chemical which is the cause for this mercury poisoning. That is, there are three types, namely, elemental, organic, and inorganic mercury. So, mercury has different effects in the body according to its chemical forms. Exposure to this chemical occurs in two ways through environmental exposure or due to occupational exposure. Different forms of mercury target different vital organs of the body, on failure of these organs are crucial for the body which might lead to the death of the individual. Diagnosis of different types of mercury poisoning can be done by analyzing the samples of hair, urine, whole blood, and certain tissues of the body. This analysis also gives us the results of recent exposure to the chemical. According to the lab diagnostic report and through preliminary clinic examination, the patient is treated according to the duration and dosage of mercury exposed to.

Keywords: Mercury poisoning, Environmental toxin, Mercury, Occupational hazards.

INTRODUCTION

Mercury is deadly metal which is known for its toxicity which might become lethal on exposure or inhalation, which was discovered for inducing public health disasters in Minamata Bay, Japan [1] and in Iraq [2-4]. The clinical features of minimal amount of exposure of mercury to an individual still remain a mystery. They exist in three definite forms. They consist of elemental mercury, inorganic mercury comprising primarily mercurous (Hg^{2+}) and mercuric salts (Hg^{++}), and organic form which comprises of mercury bonded to organic structures which consist of atoms such as carbon (like propyl and methyl groups). The chemical and biological behavior and clinical significance of different forms of mercury are different when they are bonded to different chemical structures.

Interconversion can occur between these forms to form different forms of mercury. Inhaled elemental mercury from the environment due to contamination is absorbed by the mucous layers of lungs were interconversion takes place due to oxidization to form other forms of mercury which might go and get deposited in various tissues. Certain forms of mercury-like methyl mercury are easily absorbed in gut and get deposited in many parts of the body, However, does not cross the blood-brain barrier as efficiently as elemental mercury. On entering the brain, interconversion of methyl mercury to elemental mercury takes place due to demethylation process [5]. These mercury salts, contradicting fact is that the elemental mercury is insoluble, relatively unstable and has poor absorption capability.

Human toxicity levels various with a different form of mercury. The factors, which determine the level of poisoning, are dosage and duration of exposure [5]. The long duration of exposure to elemental mercury leads to respiratory disorders such as pneumonitis, which can be extremely lethal [5]. The organ which is highly affected by mercury vapor is brain while mercurous and mercuric salts affect the tissues of gut and kidney and methylmercury affects the whole body [5].

There are considerable treatments for the mercury poisoning which includes chelation methods such as 2,3-dimercaptopropanesulfonic acid (DMPS) (Unithiol) and meso-2, 3-dimercaptosucccinic acid (DMSA) (Succinator) method. Many authors have accepted the fact that DMPS is a better chelating agent than DMSA except for one author who says that DMSA is a better chelating agent than DMPS with evidence [6].

SOURCES OF MERCURY EXPOSURE

In this widespread world, the human exposure to mercury is achieved in various elemental factor and due to day to day activities also. Some of the methods through which exposure takes place is due to outburst of mercury from the dental amalgam in the oral cavity, ingestion of contaminated fish, or through occupational exposure, according to the World Health Organization (WHO) [7,8].

The various forms of mercury are present all around us. The basic element mercury or sulfides are formed and found inside the earth's crest at a concentration of 0.5 parts per million. The atmosphere is one of the keys to exposure of mercury to humans by out bursting of volcanoes and outgassing of rocks which indeed release mercury into the environment and cause various health effects to the human. Contradicting to the fact that humans are affected, we humans are also one of the keys for exposure of mercury into the environment coal burning and mining [9].

The atmospheric mercury, which is present in the atmosphere in the elemental form on settling down into the water bodies, gets interconverted to organic form because of the microorganisms present in the water body. This organic content is ingested by the living organisms in the water bodies such as the fishes (tuna, sardines, and kingfish), which are eventually consumed by the larger creatures of the same water bodies. Due to biomagnification, the fish which is in the first level of the food might considerably have large concentration of the mercury in their tissues all over the body (Fig. 1).

Mercury exposure to human chiefly occurs through the presence of environmental mercury which inhaled by the humans through outburst of dental amalgam or occupational exposure or consumption of mercury bonded to organic substance (methyl or butyl mercury), primarily seafood.

Most of the mercury inhaled through the humans is a result of outgassing of mercury vapors from dental amalgam at the rate of 2-28 mg per facet surface per day, out if which 80% is absorbed, according to the WHO [7,8] and Berglund *et al*. [10]. A less common source of mercury vapors is spilled mercury [11], where certain disorders such as thrombocytopenic purpura [12] caused by vacuum spilled mercury.

Methyl and dimethyl mercury are originating from natural sources such as lakes and over thousands of lakes have begun closed to prevent mercury poisoning as these lakes are reservoirs for mercury which has resulted in contamination of the lakes which has also affected the fishes by biomagnification.

TOXICITY

Mercury is a poisonous metal in any form. It hinders the cellular functions by altering the tertiary and quaternary structure of the proteins by inhibiting and binding to the sulfhydryl and selenohydryl groups.

Hence, mercury can potentially impair the functions of various organs of the humans (Fig. 2).

INORGANIC MERCURY

Metallic mercury vapor

The major organ affected by metallic mercury vapor is the Brain. It also affects the renal function, immune function, peripheral nervous function, endocrine, and muscle function [13].

Exposure of mercury for a very long time at a high dosage will lead to erosive bronchitis and bronchiolitis which might eventually lead to respiratory failure accompanied by symptoms such as tremors which are associated with the central nervous system of the body [14].

Exposure to mercury vapors for a very long time might create clinically significant problems associated with neurological dysfunction. Mild exposures may cause nonspecific symptoms such as weakness, fatigue, anorexia, weight loss, and gastrointestinal (GI) disturbances [15].

High levels of exposure to mercury in high dosage might leave to clinical symptoms such as mercurial tremors, which have features of coarse shaking and fine muscle fasciculation.

Erethism may also be observed with clinical features like behavior and personality changes along with the loss of memory, insomnia, depression, fatigue, and severe cases might also cause hallucinations [10].

These diseases can be clinically diagnosed by identifying certain features in the oral cavity like the presence of gingivitis and copious salivation [5].

Mercuric mercury

Severe poisoning with mercuric salts like mercuric chloride affects many vital organs such as kidney and GI tract. A bunch of symptoms consisting of abdominal pain, dehydration, and bloody diarrhea is caused due to the precipitation of enterocyte proteins. This may produce a hypovolemic shock which ultimately leads to death. A patient who survives will develop renal tubular necrosis along with anuria [16].

Long-term mercuric poisoning is caused mainly due to the occupational exposure of mercury to human for a very long time. This affects the kidneys else the autoimmune system else affects both the systems mentioned above [16]. Immune dysfunctions have effects on human by producing hypersensitivity reactions to mercuric exposure which leads to asthma and dermatitis [17]. It also reduces the activity of the natural killer cells and other lymphocytes of the immune system [5].

Accumulation in thyroid gland decreases the free T3 levels while increase reverse T3 levels [18]. Moreover, accumulation in testicles appears to inhibit spermatogenesis [19].

Organic mercury

Methyl mercury in the body reacts with sulfhydryl group and potentially damages the intercellular structures.

It interferes with the DNA transcription indirectly affecting the protein synthesis [20] including the proteins synthesis, which is needed for brain development by the destruction of ribosomes [21].

Adverse effects are also reported on heme synthesis [22], cell membrane integrity in many locations [5].

Organic mercury is also associated with the generation of free radical mechanism which leads to cancer which is one of the deadliest diseases the whole world today is fighting against [23,24].

It creates neurological problems which damage the central nervous system by stimulation of neural excitotoxins [5] and by inferring in neurotransmitter chain.

Methyl mercury is affecting immune system by decreasing the natural killer cells [25-28] as well as creates an imbalance in th2:th1 ratio favoring autoimmunity [17,29].

Laboratory method of diagnosis

The mercury absorbed in the body gets accumulated in certain tissues such as hair, blood, fingernail, and starts increasing in concentration. It gets distributed to different body parts through blood. So, to estimate the concentration of mercury in the whole body, each and every organ must subject to measure the concentration of mercury so that whole body concentration is known. Since it is difficult and time-consuming, the common methods to find concentration levels of mercury are through testing samples such as hair, urine, fingernail, and blood. According to certain studies, the recent exposure of the mercury is seen to be correlating with the mercury samples of blood and urine [30,31]. The mean mercury concentration levels in population in whole blood and urine were observed to be 1-8 and 4-5 μg/L, respectively (Fig. 3).

Blood mercury concentration

Blood mercury concentration increases very significantly on exposure to mercury in any form. There the measurement of concentration also should take place only after the exposure to get validated authentic results [32]. However, when people are subjected to the exposures for a very long period and then even if the exposure is ceased then still the concentration of mercury levels will be high due to the presence to accumulated mercury in the body [33].

The major contribution of the concentration mercury levels in blood is due to methyl mercury which is linked with the amount of mercury we are exposed to on daily basis. The mercury concentration in whole blood is usually below 10-20 μg/L [34]. The blood mercury concentration can increase to 35 μg/L after long-term exposure to inorganic mercury due to occupational factors [34].

Urine mercury concentration

Urine mercury concentration is a very stable due to the characteristic medium. It is relatively a quick and efficient way to identify those who are exposed to mercury. Since organic mercury is significantly a small portion of the urine mercury, inorganic and metallic mercury are very effectively analyzed. People who are exposed to mercury for a long period will excrete considerable amount of mercury in urine because of the burden of mercury in the body [34]. When the urine mercury level increase 100 μg/L, the central nervous system is damaged while increased level of 800 μg/L or above is fatal to the individual [35].

Hair mercury concentration

While 80-90% of the hair composed of keratin which has high amounts of sulfhydryl groups in them. Since mercury has very high affinity to sulfhydryl group, it binds with the group and gets deposited in the hair as hair mercury. Therefore, increased exposure to mercury is seen as increased amount of hair mercury concentration. The migration of mercury to hair is irreversible, and hair mercury

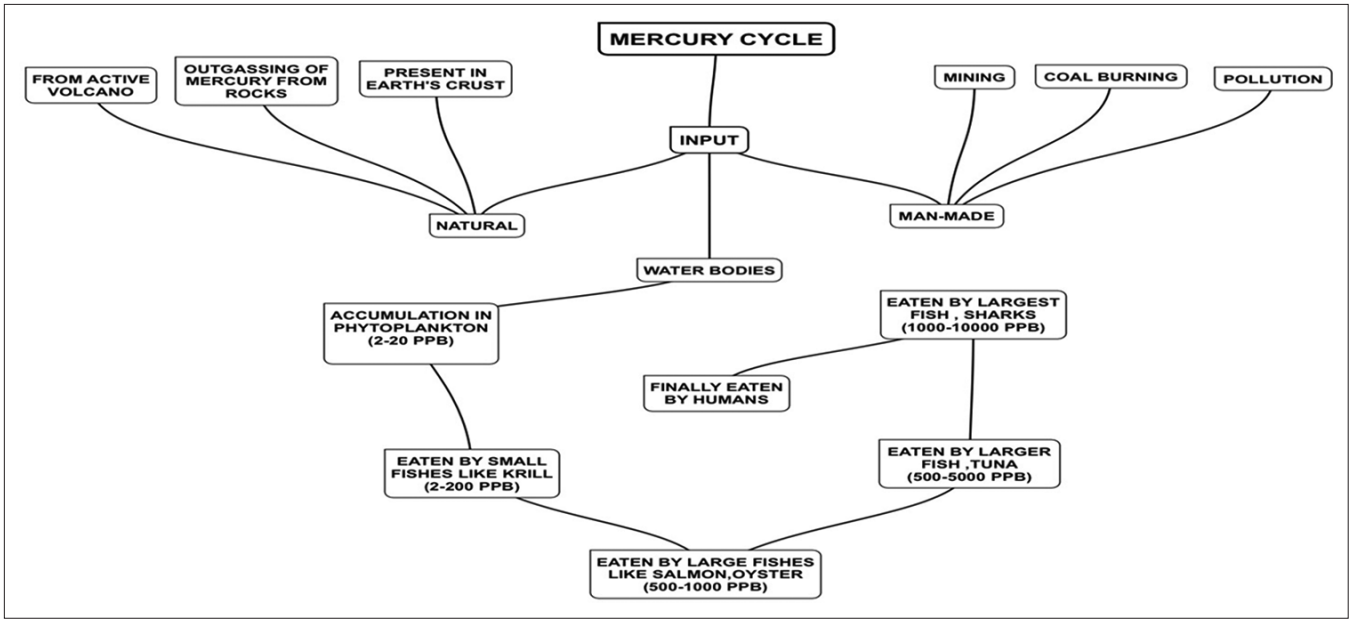

Fig. 1: Systematic representation of mercury cycle

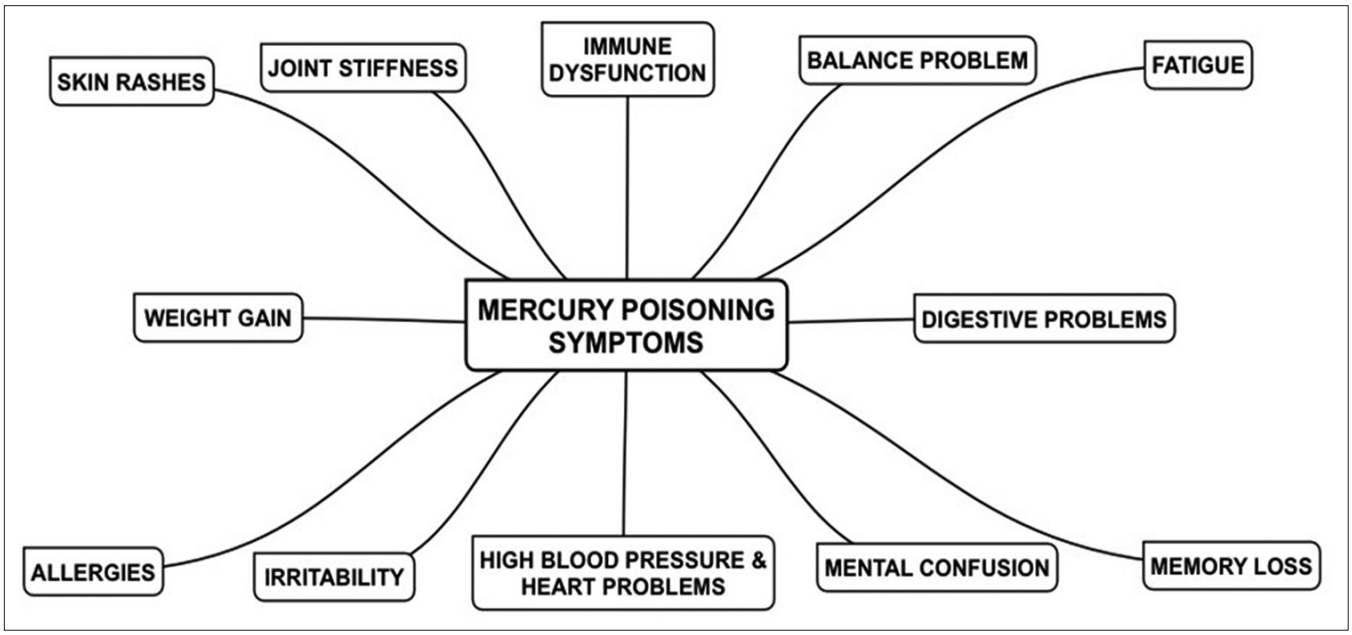

Fig. 2: Symptoms of mercury poisoning

levels are proportionate to blood mercury levels [36-38]. This can be used as a biomarker of detection for methyl mercury. A normal level of hair mercury is 10 mg/kg while in moderate poisoning its 200-800 mg/kg [39] and if it is in concentration of 2400 mg/kg then its state of intoxication.

TREATMENTS

General supportive treatment

First, an interview done with the patient to find out the cause of exposure to the patient and whether the exposure is chronic or acute, and then, perform the preliminary examinations before moving to the treatments. If the patient had inhaled the chemical, then chest X-rays has to be taken along with the arterial blood gas analysis, and if found affected then incubation and artificial ventilation have to be prepared. If it's through skin exposure, then the skin has to be washed with soap, and if eyes are contaminated, then it has to be cleansed with saline which is very necessary to prevent further infection [40].

In case of ingestion of inorganic mercury, first kidney-urinary-bladder X-ray is taken to see the movement of mercury in GI tract, and then, gastric irrigation with charcoal along with blood dialysis is performed [41].

Plasma exchange-hemodialysis-plasmapheresis

Plasma exchange has to be administered with 24-36 hrs after the mercury poisoning is diagnosed. This kind of treatment is done only when the patient is critical, and no other alternates are available. If the pollutant is dialyzable and hydrosoluble, then this is the best method. However, some toxins have a high affinity toward plasma and bind with plasma proteins and are very difficult to isolate from each other. At that situation, plasmapheresis removes heavy metals from the plasma such as mercury [42].

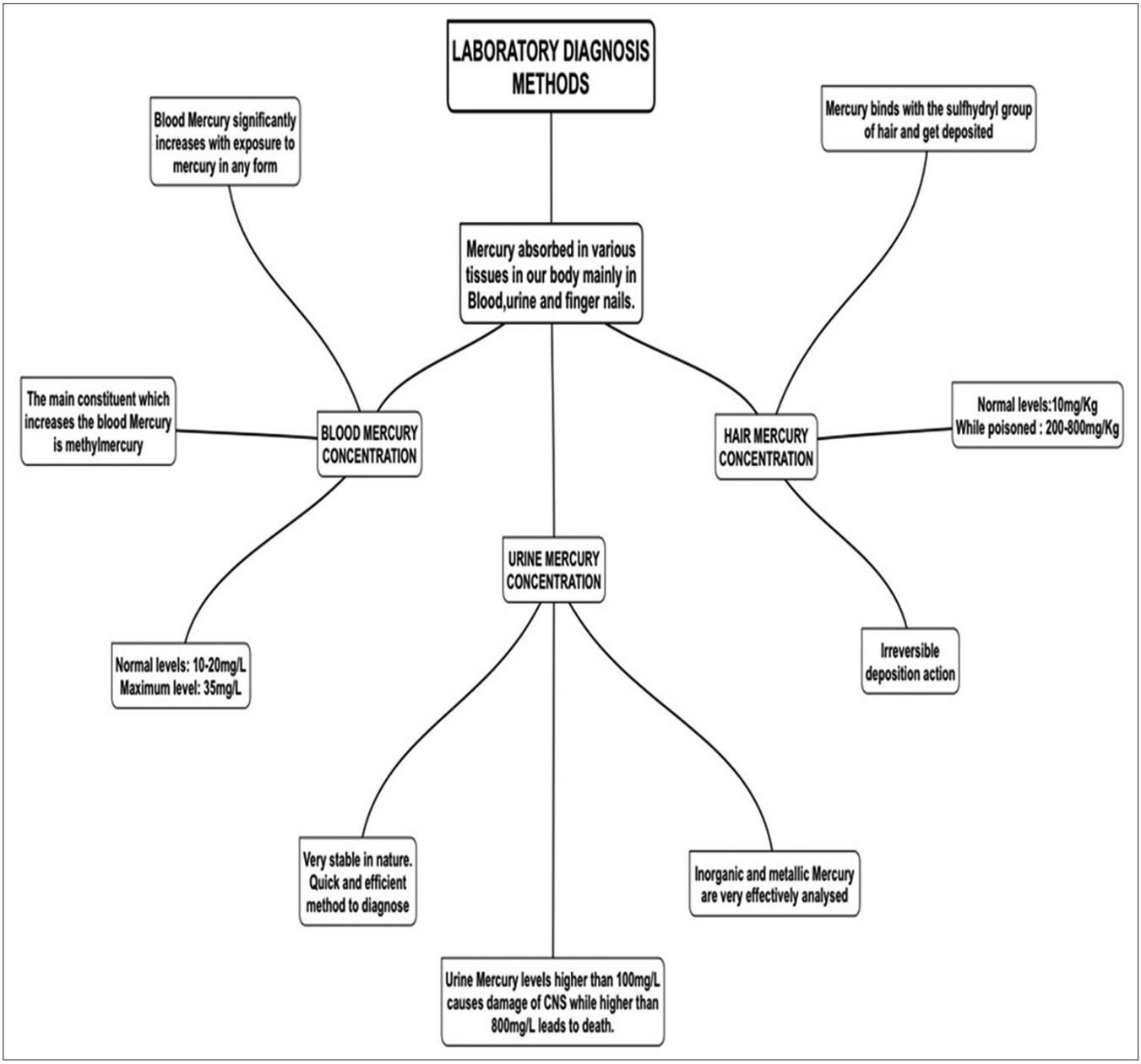

Fig. 3: Laboratory diagnosis method

Chelating agents

Patients who are diagnosed with mercury poisoning can take the chelating agent treatment. However, the use of this treatment is not advised as it has not been proven to be beneficial to patients as well has its own side effects. Chelating agents can be used to treat acute inorganic mercury poisoning. The chelation agents include very widely used D-penicillamine (DPCN), DMPS, and succimer (DMSA).

DPCN is a chelating agent used to treat metallic and inorganic mercury poisoning [43]. It increases the excretion of mercury through urine. About 250 mg of DCPN is administered to adults orally four times a day. Adverse effects of these agents include thrombopenia, leukopenia, and nephrotic syndrome. These agents have to be used with care [34].

Dimercaprol or British antilewisite can be administered through intramuscular injection which causes pain and might trigger an allergic reaction which is used as chelating agent and has a very less therapeutic use, and includes both DMPS and DMSA.

DMSA had half-life for about 3 hrs and administered orally and its absorption rate is 20%. Increases the amount of mercury excreted through urine. It is the most commonly used method for chronic methylmercury poisoning. When taken orally the adverse side effects are minimized.

DMPS has half-life of about 20 hrs and administered intravenously and has an absorption rate of about 39%. Increase the amount of excretion of inorganic and metallic mercury in urine. However, DMPS was not effective in removing methyl mercury through kidneys [44].

CONCLUSION

1. Mercury is an environmental toxin which is present all around us in our workplace, transports as well as our house in which we live. There is an increasing awareness about this chemical and its adverse poisoning effects in recent years. It was been discovered that it is not only harmful to the health of vulnerable people in society like pregnant women and children but also to ordinary adults in a large

number of ways. Studies of recent times show that a mild exposure to this deadly poison may cause cardiovascular, neurological, renal, reproductive, developmental, and carcinogenic toxicity. In the current study, we have considered all these characteristics of mercury and have given a briefing about the source, toxicity, treatment, and management techniques to help people suffering from this poisoning and to create awareness among people so that this mercury poisoning can be prevented and a lot of innocent lives can be saved.

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