REVIEW ARTICLE

USES AND EFFECTS OF MERCURY IN MEDICINE AND DENTISTRY

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Mercury is known to be a toxic material with adverse effects on the body as claimed by so many researchers and always projected a negative aspect of this element. It is true that it may cause a several problems when it exceeds the safe limit but along with its negative image, mercury has been playing a positive role in the field of medicine and dentistry. It has many therapeutic uses including various medications, ointments, dental fillings, contact lens, cosmetics, paints as well as in different instruments like thermometer and sphygmomanometers. Mercury and its compounds used in dental practice may be responsible for release of mercury into the oral cavity. Compounds of mercury tend to be much more toxic than the element itself, and organic compounds of mercury (e.g., dimethyl-mercury) are often extremely toxic and may be responsible in causing brain and liver damage.

Keywords: Mercury uses, Mercury toxicity, Dental amalgam, Elemental mercury, Dimethyl mercury

INTRODUCTION

Mercury (Latin: *hydrargyrum*, Hg, meaning water and silver) is an element with the melting point -38.83 °C and boiling point 356.73 °C.[1,2] Mercury has a narrow range of its liquid state among metals[3], and its atomic number is 80[4]. This element is naturally found in the earth's crust around 80 µg/Kg. It has been distributed throughout the environment by natural processes such as volcanic activity, fires, movement of rivers, lakes, oceanic up-welling and biological processes.[5] Most of the mercury production nowadays takes place in Spain, Kyrgyzstan, China and Tajikistan.[6] Mercury is extracted from ore cinnabar (occurring in red crystals or masses) which is mercury sulphide and mainly found in rocks that are associated with volcanic action. Generally mercury is released by heating the ore which causes sulphur to react with oxygen and is lost as sulphur dioxide gas leaving behind the metallic mercury.[7]

$$HgS+O_2 \rightarrow Hg+SO_2$$

Mercury is a naturally occurring element that may exist in elemental, inorganic or organic forms in various oxidation states.[8] When it has a zero oxidation means Hg° exists as vapours or as liquid metal state, mercurous state is a state where Hg^{+} exists as an inorganic salt whereas mercuric state Hg^{2+} may form either inorganic salts or organo-mercury compounds.[9]

Table-1: Types of mercury and their sources of exposure[10]

Type of Mercury	Source of exposure
Elemental	Dental amalgam, alkaline batteries, barometer, chloralkali plant, jewellery making, neon light, paint, paper, sphygmomanometer, thermometer, weighed nasogastric tube, accidental spillage of mercury containing devices, latex paint
Inorganic	Antiseptics, bleaching creams, calomel teething, powders, diuretics, felt hat industry, laxatives, stool fixatives
Organic	Food fish, fungicides, insecticides, grains and seeds, treated liver stock feeding on treated grains, processed woods, plastics, paper, vaccines containing thimerosal

Inorganic mercury compound: This form of mercury has been used topically in a variety of therapeutics.[11] These compounds have been used for many years in different numerous products, including various medications, germicidal soaps, teething powders and skin creams, and many of these products are still in use.[12] Calomel or mercurous chloride has traditionally been used as a diuretic, topical disinfectant and laxatives.[13] It is also known as sweet mercury and was used in infant teething powders as well as an analgesic.[14] Mercuric chloride also acts as a corrosive sublimate for treatment of syphilis[15] whereas mercuric oxide or ammoniated mercury can be used in the treatment of psoriasis.[16] Inorganic mercury creams and ointments have been used for centuries as antiseptics and to treat impetigo, lice and some inflammatory skin diseases. Some manufactures have advertised them as skin lighteners[17] but the women of childbearing age who use mercury based skin lighteners may place their unborn foetus at risk for neurological, nephrological and dermatological disorders[18]. Some of the mercury based skin whiteners contain mercury salts which may inhibit the melanin formation by competing with copper in tyrosinase.[19] Inorganic mercurial preparations may induces fatigue, insomnia, weight loss, paresthesias of the feet and hands, erythema, pruritus, excessive perspiration and hypersalivation, progressive weakness in the extremities, renal tubular dysfunction and neuropsychiatric disorders.[20]

Organic Mercury Compound: Thimerosal is an organic mercury containing compound that is 49.55% mercury by weight, and initially metabolised to ethylmercury compounds and thiosalicylate.[21] Thimerosal is an antibacterial and antifungal agent, has been used as antiseptic and preservative in different formulations including paints, topical medications, contact lens, cleaners and cosmetics since the 1930s.[22] Ethyl mercury in the form of thimerosal has been used as a topical antiseptic for children, including diphtheria

tetanus acellular pertussis (DTP), Hepatitis B and some Haemophilus influenza type b.[23] Thimerosal was used by more than 30 vaccines licensed in the United State, but due to the ingredient the problem was in discussion and finally the majority of vaccines are now free of thimerosal.[24] The derivatives of ethyl mercury are known virulent neurotoxins in nature and may responsible to produce symptoms on either acute or chronic exposures, it may be hazardous because of their ability to penetrate the epithelium and blood brains barriers, this may cause an adverse effect because of their volatility.[25] Methylmercury (MeHg) is a known neurotoxicant and its also proven the effects on the immature organism as well, with particular reference to the delayed onset of symptoms and the persistency of central nervous system (CNS) injury/dysfunction.[26]

Elemental Mercury: Different forms of mercury are used in the variety of different applications. But the elemental form of mercury is still widely used in various instruments like thermometer and sphygmo-manometers.[27] Intoxication of this form of mercury may result from inhalation or exposure to mercury dust and powder by vapours during amalgam filling or accidental ingestion of mercury from instruments, such as thermometers.[28] In direct restoration for example, mercury-silver amalgams are still widely used to fill the cavities in the posterior segment of the mouth in third world countries, while chewing the tiny amount of mercury is vapourised and reaching the olfactory bulb and brain.[29] Mercury may be released in several forms like elemental mercury vapour or metallic ions from the dental amalgam filling during chewing, tooth brushing, and para-functional activities like bruxism. The parameters of releasing the mercury vapour depends on the various different factors like number of dental amalgam fillings, the filling size and placement, chewing habits, food texture, grinding and brushing teeth, inhalation-absorption, ingestion and body weight, composition, surface and age of the amalgam restorations also a matter of concern. Therefore, there are large variations in the estimation of daily mercury absorption and release.[30] It is well documented that the main source of permanent low-level exposure from dental amalgam in the form of mercury vapour and inorganic mercury.[31]

In daily life the intake and retention of different type of mercury is inevitable for non occupational exposure to the human. Estimated average human daily intake and retention of mercury for non occupation exposure to humans are shown in Table-2.[32]

According to US Environmental Protection Agency (EPA) safety limits for mercury vapour exposure are 10 µg/day. Different studies have shown that the mercury amalgam fillings release anywhere from 1–29 µg/day, 3 times the limit. The rates of mercury release from dental amalgam restorations are dependent upon several factors including the number of amalgam restorations in the mouth, the composition of dental amalgam (high *vs* low copper dental amalgam), the location of the amalgam restoration also play an important role (occlusal *vs* non-occlusal teeth), including the amalgam surface area.[33] Some scientists agree that dental amalgam fillings leach out the mercury into the mouth and according to FDA studies showed that this may be as low as 1–3 µg/day or as high as 27 µg/day.[34] The safety limits for fish and seafood are 2.3 µg/day and the other foods are 0.3 µg/day whereas air or water values are negligible respectively.[33]

Mercury toxicity has been a cause of concern for the researchers and the health safety organisations for many years. It is said that mercury toxicity from different exposure may cause some serious illnesses and may be responsible to effect on the different organ of a body.[35] Toxic dose and effects on a different organ of a body are shown in Table-3.

Table-2: Daily intake and retention (µg/day) of various types of mercury

Source of exposure	Daily intake and retention (µg/day) of various types of mercury		
	Elemental	Inorganic	Methyl mercury
Air	0.04–0.2	Minimal	0.0080 (0.0069)
Dental amalgam	1.2–27 (1–21.6)		0
Food-Fish (100 g/ week containing 0.2 mg Hg/Kg)	0	0.60 (0.06)	2.4 (2.3)
Other	0	3.6 (0.36)	0
Drinking Water	0	0.05 (0.005)	0
Total	1.2–27 (1–22)	4.3 (0.43)	2.41 (2.31)

Table-3: Effect of different types of mercury on human organs

Human organ system	Toxic dose of different types of mercury		
	Elemental	Inorganic	Organic
Neuromuscular and neurological	40–60 µg/L urine (Acute) 500 mg/m^3 urine (chronic)	>50 mg/m^3 urine (chronic)	100–200 µg/dL blood (acute)
Kidney	>5–10 µgHg/g creatinine urine (chronic)	>5–10 µg Hg/g creatinine urine (chronic)	
Thyroid	15–30 µg/g creatinine urine (chronic)		
Reproductive system			33.2 µg Hg/m^3 blood

The liquid form of mercury is not to be easily absorbed whereas the vapours can be metabolised. The symptoms may depend on the exposure of mercury poisoning whether is acute or chronic. Acute toxic effects are generally anticipated at levels of 50 µg Hg/L blood or 100 µg Hg/L urine, compared with normal (no effect) levels of up to 10 µg Hg/L blood or 10 µg Hg/L urine in humans.[36] Acute toxicity may affect the different systems including the kidneys, GI tract, lungs, nervous and immune systems.[37] Chronic exposure of humans to elemental or inorganic mercury, such as might be experienced in some occupational situations,

has been shown to result in persistent damage to the central nervous system and a wide range of effects including progressive anaemia, gastric disturbance, excessive salivation, metallic taste in the mouth and tenderness of the gums.[38] The nervous system is known to be the most sensitive target organ and produced the neurological problems (such as tremor, insomnia, polyneuropathy, paresthesia, emotional ability, irritability, personality changes, headache, weakness, blurred vision, dysarthria, speech impairment, slowed mental response and unsteady gait) have been reported in adults. Pre- or postnatal exposure to high levels of MeHg may cause mental retardation, cerebral palsy, and seizures. Kidneys are particularly susceptible to mercury salts resulting in different pathological changes such as acute tubular necrosis and immunologic glomerulo-nephritis; this may also be responsible to cause arrhythmias and cardiomyopathy.[39]

Quantitative data on different mercury concentrations in blood, urine and elemental mercury inhalation exposure, have already been established and including the early effects of mercury toxicity. The non-specific symptoms of micromercurialism are observed on long term exposures to elemental mercury, air concentrations of 50 μg/m^3, or at 35 μg/L in blood, or 150 μg/L in urine. Overt neurotoxicity (tremor) occurs after long term inhalation of elemental mercury at concentrations 100–200 μg/m^3 with resulting blood mercury concentrations of 70–140 μg/L and urinary mercury in the range of 300–600 μg/L.[30] Different analysis methods are using to measure the mercury levels in the biological samples but the cold vapour atomic absorption spectrometric (CVAAS) analysis is the most common method used to measure mercury levels.[40]

Mercury compounds tend to be much more toxic than the elemental mercury itself, and the organic compounds of mercury are often extremely toxic and may be responsible in causing brain and liver damage. The most dangerous mercury compound is dimethylmercury.[41] Dimethylmercury is a volatile liquid organic mercury compound, and is used by a small number of chemistry laboratories as a reference materials, such as nuclear magnetic resonance spectroscopy.[42] The lethal dose of dimethylmercury is approximately 400 mg of mercury (equivalent to a few drops, or about 5 mg/Kg of body weight) and is supertoxic.[43] Since it is a highly toxic compound so the precautions should be taken in handling this compound because even a few μL spilled on the skin, or even a latex glove, can cause death.[44] The acute lethal dose of mercuric chloride is approximately 1–4 g and the fatal dose in humans is approximately 100 mg organic mercury or 1 g mercury salt.[45,46]. Liquid metallic mercury is poorly absorbed from gastrointestinal tract and acute ingestion has been associated with poisoning only in the presence of normal gut mobility that markedly delays normal faecal elimination or after peritoneal contamination.[47] The symptom of respiratory distress may be produced at 1.1–44 mg/m^3 (equivalent urine levels of 169–520 μg/L), but the potential lethal dose of elemental mercury is well tolerated orally up to 240 g.[35]

There are different organizations which are concerned with health effects and toxicity or allergy associated with exposure to mercury. They follow up the exposure and consumption according to standard limits to make sure not to exceed the safety limits.[48] No such organizations are available in Pakistan. There is need to amend law for the safety and control.

REFERENCES

1. Grimes IC, Einarsson S, Spier BJ, Reichelderfer M. Mercury ingestion retrieved by colonoscopy. Gastrointest Endosc 2009;70:559–60.
2. Grolier JPE, Dan F. The use of advanced calorimetric techniques in polymer synthesis and characterization. Thermochim Acta 2006;450(1–2):47–55.
3. Fu Z, Wu F, Amarasiriwardena D, Mo C, Liu B, Zhu J, *et al*. Antimony, arsenic and mercury in the aquatic environment and fish in a large antimony mining area in Hunan, China. Sci Total Environ 2010;408:3403–10.
4. Kristi L. Understanding the element of the periodic table Hg. 1st ed. USA: Rosen Publishing Group; 2009.p 17.
5. World Health Organization International Programme on Chemical Safety (WHO IPCS). Concise International Chemical Assessment Documents 50. Elemental mercury and inorganic mercury compounds human health aspects; 2003 Report. available at www.who.int/ipcs/publication/cicad/en/cicad50.pdf.
6. Hylander LD, Meili M. 500 Years of mercury production global annual inventory by region until 2000 and associated emissions. Sci Total Environ 2003;304:13–47.
7. Emsley J. The element of murder, 1st ed. New York: Oxford University Press Inc; 2005.p. 48.
8. Gochfeld M. Cases of mercury exposure, bioavailability, and absorption. Ecotoxicol Environ Saf 2003;56:174–9.
9. Clifton JC 2nd. Mercury exposure and public health. Pediatr Clin North Am 2007;54(2):237–69.
10. Bose-O'Reilly S, McCarty KM, Steckling N, Lettmeier B. Mercury exposure and children health. Curr Probl Pediatr Adolesc Health Care 2010;40(8):186–215.
11. Goldman LR, Shannon MW. American Academy of Pediatrics: Committee on Environmental Health. Technical report: Mercury in the environment: implications for pediatricians. Pediatrics 2001;108:197–205.
12. Guzzi G, La Porta CA. Molecular mechanisms triggered by mercury. Toxicology 2008;244(1):1–12.
13. Dyall-Smith DJ, Scurry JP. Mercury pigmentation and high mercury levels from the use of a cosmetic cream. Med J Aust 1990;153:409–15.
14. Weinstein M, Bernstein S. Clinical Vistas: Pink ladies: mercury poisoning in twin girls. CMAJ 2003;168:201.
15. O'Shea JG. Two minutes with venus, two years with mercury – mercury as an antisyphilitic chemotherapeutic agent. J R Soc Med 1990;83:392–5.
16. Bruce AF, Margaret HW, Carl GE. Mercury induced renal effects. J Clin Nephrotox 2008;3:811–26.
17. Boyd AS, Seger D, Vannucci S, Langley M, Abraham JL, King LE Jr. Mercury exposure and cutaneous disease. J Am Acad Dermato 2000;43:81–90.
18. Yoshida M, Satosh M, Shimada A, Yamamoto E, Yasutake A. Maternal-to-fetus transfer of mercury in metallothionein-null

pregnant mice after exposure to mercury vapour. Toxicol Pathol 2002;175:215–22.
19. Dadzie OE, Petit A. Skin bleaching: highlighting the misuse of cutaneous depigmenting agents. J Eur Acad Dermatol Venereol 2009;23(7):741–50.
20. Counter SA, Buchanan LH. Mercury exposure in children: a review. Toxicol Appl Pharmacol 2004;198:209–30.
21. Tan M, Parkin JE. Route of decomposition of thimerosal. Int J Pharm 2000;208:23–34.
22. Geier DA, Sykes LK, Geier MR. A review of Thimerosal (Merthiolate) and its ethylmercury breakdown product: specific historical considerations regarding safety and effectiveness. J Toxicol Environ Health B Crit Rev 2007;10:575–96.
23. Young HA, Geier DA, Geier MR. Thimerosal exposure in infants and neuro developmental disorders: An assessment of computerized medical records in the Vaccines Safety Data link. J Neurol Sci 2008;271(1-2):110–8.
24. Rennels M, King JJ, Ryall R, Papa T, Froeschle J. Dosage Escalation, Safety and Immunogenicity Study of Four Dosages of a Tetravalent Meninogococcal Polysaccharide Diphtheria Toxoid Conjugate Vaccine in Infants. J Pediatr Infect Dis 2004;23(5):429–35.
25. Gosselin RE, Smith RP, Hodge HC, (Eds). Clinical Toxicology of Commercial Products. (5th ed). Baltimore: Williams and Wilkins; 1984. p. 267.
26. Castoldi AF, Onishchenko N, Johansson C, Coccini T, Roda E, Vahter M, *et al*. Neurodevelopmental toxicity of methylmercury: Laboratory animal data and their contribution to human risk assessment. Regul Toxicol Pharmacol 2008;51:215–29.
27. Halbach S, Vogt S, Köhler W, Felgenhauer N, Welzl G, Kremers L, *et al.* Blood and urine mercury levels in adult amalgam patients of a randomized controlled trial: Interaction of Hg species in erythrocytes. Environ Res 2008;107:69–78.
28. Ye X, Qain H, Xu P, Zhu L, Longnecker MP, Fu H. Nephrotoxicity, neurotoxicity, and mercury exposure among children with and without dental amalgam fillings. Int J Hyg Environ Health 2009;212:378–86.
29. Thomas WC, Laszlo M. The Toxicology of Mercury and Its Chemical Compounds. Crit Rev Toxicol 2006;36:609–62.
30. The safety of dental amalgam and alternative dental restoration materials for patients and users. Scientific Committee on Emerging and Newly Identified Health Risks SCENIHR. The SCENIHR adopted this opinion via written procedure on 6 May 2008, after consultation. Available at: http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scnihr_mi_016.pdf
31. Ozdabak HN , Serpil K, lanog L, Nilgu A , Fevzi P, Nilgu. The effects of amalgam restorations on plasma mercury levels and total antioxidant activity. Arch Oral Biol 2008;531:1101–6.
32. WHO (World Health Organisation).Mercury in drinking water. Back ground document for development of WHO guidelines for Drinking water Quality. Document WHO/SDE/WSH/05.08/10, 2005.Geneva, World Health Organisation. Available at: www.who.int/water_sanitation_health/dwq/chemical/mercuryfinal.pdf
33. World Health Organization, Environmental Health Criteria 118: Inorganic mercury, Geneva, 1991. Published under the joint sponsorship of the United Nations Environment Programme, the International Labour Organisation, and the World Health Organization First draft prepared by Dr. L. Friberg, Karolinska Institute, Sweden World Health Orgnization Geneva, 1991.
34. Dental Amalgam: Myths vs Facts CHICAGO, 2002 Americian Dental Association. http://www.nysdental.org/img/uploads/file/filfacts.pdf
35. Holmes P, James KAF, Levy LS, Is low level environmental mercury exposure of concern to human health. Sci Total Environ 2009;408:171–82.
36. Caravati EM, Erdman AR, Christianson G, Nelson LS, Woolf AD, Booze LL, *et al.* Elemental mercury exposure: An evidence-based consensus guideline for out-of-hospital management. Clin Toxicol (Philla) 2008;46(1):1–21.
37. EU (European Union Employment and Social Affairs. Health and Safety at Work). Recommendation from the Scientific Committee on occupational exposure limits for elemental mercury and inorganic divalent mercury compounds; 2007. Available at: http://ec.europa.eu/employment_social/health_safety/recommendations_en.htm.
38. Boadi WY, Urbach J, Brandes JM, Yannai S. In vitro effect of mercury on enzyme activities and its accumulation in the first-trimester human placenta. Environ Res 1992;57:96–106.
39. Tchounwou PB, Ayensu WK, Ninashvili N, Sutton D. Environmental exposure to mercury and its toxicopathologic implications for public health. Environ Toxicol 2003;18:149–75.
40. Murphy J, Jones P, Hill SJ. Determination of total mercury in environmental and biological samples by flow injection cold vapour atomic absorption spectrometry. Spectrochimica Acta Part B 1996;51:1867–73.
41. Joshi D, Mittal DK, Shukla S, Srivastav AK.Therapeutic potential of N acetylcysteine with antioxidants (Zn and Se) supplementation against dimethylmercury toxicity in male albino rats. Exp Toxicol Pathol 2012;64(1–2):103–8.
42. Siegler RW, Nierenberg DW, Hickey WF. Fatal poisoning from liquid dimethylmercury: A neuropathology study. Hum Path 1999;30:720–3.
43. Nierenberg DW, Nordgren RE, Chang MB, Siegler RW, Blayney MB, Hochberg F, *et al*. Delayed Cerebellar Disease and Death after accidental exposure to dimethylmercury. N Engl J Med 1998;338:1672–6.
44. Blayney MB, JS Winn, and DW Nierenberg. "Letters; Chemical Safety-Handling Dimethylmercury" Chemical and Engineering News (1997, May 12):7.
45. US Environmental Protection Agency. Summary Review of Health Effects Associated with Mercuric Chloride: Health Issue Assessment. EPA/600/R-92/199. Office of Health and Environmental Assessment, Washington, DC. 1994.
46. Bidstrup PL (Ed) Toxicity of mercury and its compounds. Amsterdam: Elsevier; 1964.p. 8–14.
47. Oslon KR (Ed). Poisiong and Drug Overdose. 4th ed. USA: McGraw Hill; 2003. p. 254.
48. Newland MC, Elliott MP, Miranda NR. Methylmercury and nutrition: Adult effects of fetal exposure in experimental models. Neurotoxicology 2008;29(5):783–801.

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