

MERCURY

Introduction

The element mercury (Hg) is a potent neurotoxin which can also have toxic effects in any organ to which it is transported. Human exposure to mercury is nevertheless commonplace and comes from environmental, food and occupational sources. Mercury was for centuries a component of many different pharmaceuticals, such as diuretics, antibacterial agents, antiseptics, and laxatives. *Amazingly, to this day, it is still used as a preservative in many vaccines.* Mercury toxicity in environmental pollution is currently a major concern because of the continued use of mercury-containing fossil fuels and agricultural products. Before 1990, many paints contained mercury as an antimildew agent. In medicine, mercury is used in dental amalgams and various antiseptic agents. Of particular concern is the consequences of the long-term intake of methyl mercury in food, due to its efficient absorption from the gut (90%), long half life in the human (70 days) and ability to cross lipid membranes and accumulate in the brain [1].

Mercury can be found in three forms:

- 1) elemental Hg^0 (which is liquid at room temperature),
- 2) inorganic Hg, with two valencies - mercurous Hg^{1+} or mercuric Hg^{2+} , with Hg^{2+} being the more toxic,
- 3) organic Hg - aryl, alkyl or alkoxalkyl, with short chain alkyl Hg being the most toxic [1].

The toxicological actions of each form are somewhat different from the others, but from the above it is evident that mercury also has transitional metal activity and can take part in electron transfer reactions (such as the Haber-Weiss reaction). These reactions are associated with the generation of free radical species and so mercury in the body can contribute to the development of oxidative stress states.

Physiological actions of mercury

No essential physiological function has been proposed for mercury. Its biochemical properties appear to derive from binding to sulphhydryl (SH) groups in proteins, membranes and enzymes [1], causing a disruption in the function of associated molecules and structures; it also forms stable complexes with amino and carboxyl groups.

For a number of elements including inorganic and organic mercury, lead and cadmium, the main route for elimination from the body is via biliary excretion into the stools [2]. Renal excretion of mercury is poor. Chronic exposure to mercury results in its accumulation within the brain, causing CNS effects, which have been well described since the 18th century. In 1961, researchers in Japan correlated ingestion of methyl mercury and elevated urine mercury levels with the features of Minamata disease [1].

Environmental sources of mercury

Current research in atmospheric science has shown how pollutants can be transported from country to country, creating health effects far from the point of emission [3]. Satellite studies of dust transport over the Pacific ocean show that emissions from Asia can reach North America in 2 weeks. Circumpolar transport at northern mid-latitudes can carry air pollutants between Asia, North America and Europe within a month. The implication of these studies is that pollutants (such as mercury) with a lifetime of more than a few weeks can be deposited around the globe in countries downwind of their origin [3,4]. Inorganic mercury emissions have an atmospheric residence time of around one year and hence are widely recognised to be transported worldwide from country to country [5].

These findings show that emissions in polluting countries have the capacity to spread mercury throughout the globe, without regard for national or continental boundaries and with deleterious effects on human health.

Food sources of mercury

Inorganic mercury can be converted by the action of methylating bacteria to methyl mercury, which has been shown to accumulate in the marine food chain. Fish at the top of this food chain (such as tuna and

swordfish) accumulate methyl mercury in their tissues and it appears that consumption of these fish by humans can significantly raise blood mercury levels. Consumption of contaminated fish is now thought to be the main source of human exposure to mercury and exposure to methyl mercury can have adverse neurological effects, especially in the developing brains of fetuses, infants and children [6].

Methyl mercury from fish has been linked to neurological damage (Minamata disease) [1] and also to an increased risk of myocardial infarction [7]. The possible mechanism for this is via mercury's action in raising blood pressure, which was experimentally investigated by Wakita in 1987 [8], who observed that rats chronically exposed to methyl mercury developed systemic hypertension that persisted for many months after exposure. Mercury could affect blood pressure by different mechanisms – via calcium homeostasis and an increase in intracellular calcium status, or by increasing oxidative stress, which leads to a reduction in nitric oxide availability, endothelial dysfunction and decreased smooth muscle relaxation.

A recent epidemiological study [9] has linked exposure to mercury to a rise in blood pressure among Nunavik Inuit men and women in northern Quebec, with blood mercury levels of more than 50 nmol/L, more than 10 times higher than the median level in the US population (4 nmol/L) as reported by the National Health and Nutrition Examination Survey (NHANES) study. These higher levels are a consequence of the preponderance of fish and marine mammals in the traditional Inuit diet. Every 1% increase in blood mercury levels was found to be associated with a 0.02-mm-Hg increase in systolic blood pressure. The adverse blood pressure of mercury effects persisted statistically as a risk factor even when the nutritional benefits of enhanced omega-3 fatty acid and selenium consumption from fish were taken into account.

A recent unique intervention study in Japan [10] used heart rate variability as a reflection of cardiac events in 54 adults. The subjects were divided into an experimental group and a control group. The experimental group was fed methyl mercury at the level of the provisional tolerable weekly intake (PTWI), as determined by the World Health Organization, through consumption of tuna and swordfish for 14 weeks, while the control group was maintained on a fish-free diet. Heart rate variability (HRV) was compared between the two groups. In the experimental group, mean hair mercury levels, determined before and after the dietary methyl mercury exposure and after a 15-week wash-out period following the cessation of exposure, were 2.30, 8.76 and 4.90 µg/gm, respectively. The sympathovagal balance index of HRV was significantly elevated after the exposure, and decreased to the baseline level at the end of the study. Changes in HRV were not observed in the control group, who had a mean hair mercury level of 2.1 µg/gm. The authors' conclusion was that the PTWI does not appear to be safe for adult health since methyl mercury exposure from fish consumption induced a temporary sympathodominant state. Long-term exposure to methyl mercury may thus pose a potential risk for cardiac events involving sympathovagal imbalance among fish-consuming populations.

Occupational exposure to mercury

The commonest form of occupational exposure to mercury is from Hg⁰ vapour. In addition to the hazards of exposure in fluorescent tube manufacturing, in mining and in the chloralkali industry, dental and medical health professionals may be exposed to Hg⁰ vapour from contaminated carpets and from the preparation and handling of amalgam fillings. Gold miners in the Amazon basin have been reported to show a variety of neurological and renal effects associated with volatilization of mercury vapour, while neurological effects typical of methyl mercury exposure have been reported among native Indian populations living next to these gold mining areas of the Amazon basin [1].

Avoidable exposure to mercury

Common sources of mercury prior to its legislated removal from such preparations were calomel-containing anthelmintics, laxatives, nappy rinse aids, teething powders, termite-protected wood (mercury bichloride), mercurial antibacterial ointments and mercurial skin-lightening creams. Thimerosal or 2-(ethylmercuriomer-capto) benzoic acid sodium salt has been commonly used as a preservative in vaccines, some of which (for example gamma-globulin as a non-specific vaccine for bacterial hepatitis) have been administered on a repeated basis. The use of mercury in dental amalgams remains a cause for concern

among many dentists as well as among the general population. Dentists are occupationally exposed to mercury and many dentists have a high body burden of mercury, and thus all dentists should be tested accordingly.

Patient preparation:

No special preparation is required prior to sampling for mercury analysis. The patient can continue to take nutritional supplements and medication before the collection of the sample.

Specimen requirements

For blood mercury measurement, the sample should be collected into an 8 ml trace element-free potassium EDTA tube. Collection tubes and needles can be supplied by the laboratory. If a number of blood tubes are being taken at the same collection, the trace element-free tube should be filled first to avoid cross-contamination. Postal samples (overnight delivery) are acceptable.

A 24-hour urine collection is preferred for urine mercury determination, because urinary elimination of mercury is unpredictable and may vary from hour to hour. The total volume collected should be recorded and, after mixing the collection, 15 mL of urine should be submitted in a plastic, screw cap container. A postal sample kit can be supplied.

For hair analysis, hair should be cut from the nape of the neck, as close to the scalp as possible. At least 0.25gm of hair is required, which is about one heaped tablespoon full. Only hair up to 1½" (4cm) from scalp can be used. Please allow for this when the hair is long by sending in a larger total sample, for example 2 tablespoons-full of hair.

Interpretation of results

Mercury is a toxic metal with no known biological essentiality in man and its presence in any concentration can be regarded as harmful under certain circumstances.

The reference intervals for mercury are as follows:

Urine Hg (for monitoring the body burden of Hg)	<2.00✓mol/mol of creatinine
Whole blood Hg (for recent exposure)	Acceptable adult range < 50.0 nmol/L (10.0 µg/L) [11]. Unexposed range for adults < 15.0 nmol/L (3.0µg/L). Unexposed range for children < 6.0 nmol/L (1.2 µg/L) [12].
Hair Hg (reflects 3 months' exposure to Hg)	< 1.00 µg/gm of hair

The deposition of mercury in hair is thought primarily to reflect exposure to organic mercury, for example from fish consumption; mercury from the diet is thus deposited in hair to minimize its adverse health effect.

There is no clearly defined reference interval for the increment in mercury production post DMSA; ideally the molar mercury/creatinine ratio in the basal urine sample should be less than 0.50, while that in the DMSA-provoked sample should be less than 1.00. The reference interval quoted on the report for the basal urine mercury/creatinine ratio (less than 2.00) reflects the current excessive dietary and environmental intake of mercury in this population. However, a "normal" DMSA provocation test result (i.e. no excessive body mercury present) can be taken as an increase in urine mercury (corrected for creatinine concentration) of less than 100 % (= twice the initial value) and below 2.00 µmol Hg per mole of creatinine. Note DMSA is not supplied by Viva Health Laboratories and should be provided by a medical practitioner for toxic element challenge testing.

Turn around time: 5 working days.

References:

1. Berlin M, Zalups RK, Fowler BA. Mercury. In: Handbook on the toxicology of the metals, 3rd edition. Eds: Nordberg GF, Fowler BA, Nordberg M, Friberg LT Elsevier, publishers, Amsterdam 2007; pp 676-729.
2. Bjorkman L, Sandborgh-Englund G, Ekstrand J. Mercury in saliva and faeces after removal of fillings. *Toxicol Appl Pharmacol* 1997;144:156-162.
3. Liu J, Mauzerall DL, Horowitz LW. Evaluating inter-continental transport of fine aerosols (2) global health impacts. *Atmos Environ* 2009;43:4339-4347.
4. Saikawa E, Naik V, Horowitz LW, et al. Present and potential future contributions of sulphate, black and organic carbon aerosols from China to global air quality, premature mortality and radiative forcing. *Atmos Environ* 2009;43:2814-2822.
5. Pacyna EG, Pacyna JM, Steenhuisen F. Global anthropogenic mercury emission inventory for 2000. *Atmos Environ* 2006;40:4048-4063.
6. NAS. Toxicological effects of methyl mercury. Washington DC: National Academic Press, 2000.
7. Guallar E, Sanz-Gallardo PHM, van't Veer P, et al. Mercury, fish oils and the risk of myocardial infarction. *N Engl J. Med.* 2002;347:1747-1754.
8. Wakita Y. Hypertension induced by methyl mercury in rats. *Toxicol Appl Pharmacol* 1987; 89: 144-147.
9. Valera B, Dewailly E, Poirier P. Environmental mercury exposure and blood pressure among Nunavik Inuit adults. *Hypertension* 2009;54:981-986.
10. Yaginuma-Sakurai K, Murata K, Shimada M et al. Intervention study on cardiac autonomic nervous effects of methylmercury from seafood. *Neurotoxicology and Teratology* 2010;32:240-245.
11. Sue YJ. Mercury. In: Goldfrank LR, Flomenbaum ME, Lewin NE, Howland MA, Hoffman RS, Nelson LS eds. *Goldfrank's toxicologic emergencies*. 7th ed. New York, NY. McGraw-Hill, pubs, 2002:1239.
12. Centers for Disease Control and Prevention (CDC) 2005. Third national report on human exposure to environmental chemicals. <http://www.cdc.gov/exposurereport/pdf/thirdreport.pdf>
13. Drinking Water Inspectorate, 55 Whitehall, London SW1A 2EY <http://www.dwi.gov.uk>