Mercury, the elusive heavy metal

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ABSTRACT

Mercury is ubiquitous in the environment and therefore every human being, irrespective of age or location, is exposed to one form of mercury or another. The major source of environmental mercury is natural degassing of the earth’s crust, whilst industrial activities can raise exposure to toxic levels directly or through the use of liquid metals or synthesised mercurial compounds.1 Mercury still gives rise to accidental and occupational exposure. The aim of this mini review is to describe the main factors that influence mercury toxicity and provide a framework for the interpretation of mercury.

INTRODUCTION

Mercury (Hg) is a heavy metal noted for inducing public health disasters – Minamata Bay in Japan, Iraq,2 and South Africa.3 Mercury exists in several forms: inorganic mercury which includes metallic mercury (Hg0) and mercury vapor (Hg); mercurous mercury (Hg2++) or mercuric salts; and organic mercury which includes methyl and ethyl mercury. Human toxicity varies with the form of mercury, the dose and the rate of exposure. The target organ for inhaled mercury is primarily the brain, whilst mercurous mercury and mercuric salts chiefly damage the gut lining and kidney.3

Human mercury exposure occurs mainly through the inhalation of elemental mercury via occupational or dental amalgam exposure and through the ingestion of mercury bonded to organic moieties (ethyl, methyl, dimethyl mercury), primarily from seafood.2 Dental amalgams emit mercury vapour which is inhaled and absorbed into the bloodstream, while liquid metallic mercury still finds its way into homes, causing a risk of poisoning from the vapour and creating major clean-up costs.2 Amongst humans, the sole source of exposure to methyl mercury (organic mercury) is through the consumption of fish and sea mammals. It has been reported that over 3000 lakes in the US have been closed to fishing due to mercury contamination.3

PHARMACOKINETICS OF MERCURY

Due to its volatility, metallic mercury (Hg0) is responsible for most cases of inhalational exposure. On entry to the body, mercury vapour is oxidised to mercuric mercury. This conversion process, however, is not rapid enough to prevent Hg0 from crossing the blood brain barrier. Metallic mercury passes easily through the blood brain barrier and the placenta, where it lodges in the foetal brain. The excretory half-lives of metallic mercury and mercuric mercury vary widely, with values ranging from a few days to several months.

Mercurous mercury salt in the form of Hg2Cl2 (calomel) is poorly soluble in water and is therefore associated with low toxicity following oral ingestion. Mercuric mercury, typically HgCl2, generally targets the gastro-intestinal tract and the kidneys. In acute poisoning cases, patients present with abdominal pain, vomiting and bloody diarrhoea, with potential necrosis of the gut mucosa. This may produce death, from peritonitis, septic or hypovolemic shock.3 Mercuric mercury does not cross the blood brain barrier efficiently but it does accumulate in the placenta, foetal tissue and amniotic fluid.3 The major burden of mercuric mercury resides in the proximal convoluted renal tubule, while brain dysfunction is less evident than with other forms of mercury.

Most available data on organic mercury refer to methyl mercury which is a major source of human mercury exposure. Mercury attached to aquatic sediments is subject to microbial conversion to methyl mercury, whereupon it enters the aquatic food chain. It reaches its highest concentration in long lived predatory fish, such as sharks.2 Once fish and sea mammals are consumed; methyl mercury is deposited throughout the body. Concentration occurs in the brain, liver, kidney, placenta and foetal brain, as well as in the peripheral nerves and bone marrow.3 The excretory half-life of methyl mercury is 70 days, with approximately 90% being excreted in stools.3

Ethyl mercury (thimerosal) is a water soluble compound used as a preservative. It is added to many commercial products, including vaccines. Ethyl mercury appears to be less toxic than methyl mercury, in part as metabolism is more rapid. Low dose ethyl mercury derived from thimerosal in vaccines has been shown to have a blood half-life of 7 days (95% Confidence Interval: 4-10 days) in 40 full term infants.4

CLINICAL PRESENTATION AND TOXICITY

The chief target organ of metallic vapour is the brain. With significant acute exposure, bronchitis and bronchiolitis, potentially leading to respiratory failure, may be accompanied by CNS symptoms such as tremor and erethism.

With low levels of chronic exposure, non-specific symptoms such as weakness, fatigue, anorexia, weight loss and gastrointestinal tract disturbances have been described. Higher levels of chronic exposure are associated with mercurial tremor, erethism, personality and behaviour changes, insomnia, loss of memory, depression, fatigue and, in severe cases, delirium and hallucinations. Gingivitis and copious salivation have also been described.3

The brain is also the primary organ affected by methyl mercury exposure. Adults present with paraesthesia of the circumoral area, hands and feet, followed by visual field constriction and ataxia.2 A major concern of methyl mercury exposure is in the prenatal period, with the foetal brain being more susceptible to mercury induced damage. Massive prenatal poisoning may induce a form of cerebral palsy, while lesser prenatal doses have been associated with neurodevelopmental delays and cognitive deficits.5 It is for this reason that the FDA has recommended that pregnant women, nursing mothers and young children avoid eating fish with a high mercury content (> 1 ppm), such as shark, swordfish, tilefish, whale and king mackerel.2

BIOLOGICAL MONITORING OF MERCURY

Analysis of mercury in blood and urine requires either atomic absorption spectroscopy hydride system or the more selective inductive coupled plasma mass spectroscopy. Several studies have demonstrated a correlation between the intensity of recent exposure to
mercury vapour and the concentration of mercury in blood, urine and saliva. Such a relationship only holds when the exposure has lasted one year. Under chronic exposure conditions, a relationship between blood or urinary Hg concentrations and the occurrence of clinical and biological signs of intoxication by mercury vapour also exists. In persons non-occupationally exposed to mercury, the concentration of mercury in urine is < 5 μg/g creatinine, and 2 μg/L in blood.

**Urinary Hg**

In newly exposed workers, urinary excretion does not immediately follow the onset of exposure; there is a latent period during which the body accumulates a certain quantity of mercury, mainly in the kidney. Nephropathological effects of mercury have been known for years and are largely dependent upon the chemical form of mercury exposure. A correlation has been demonstrated between the urinary excretion of mercury and the prevalence of neuropsychomotor effects or the prevalence of increased excretion of urinary proteins. Some authors have reported an increased prevalence of slight tremor and biological signs of renal dysfunction in workers excreting > 50 μg/g creatinine of Hg, while other data suggest that exposure to metallic mercury < 5 μg/m³ which leads to urinary excretion values below 35 μg/g creatinine may still increase finger tremors.

The value of 50 μg/g creatinine has been proposed and endorsed by the World Health Organization (1980) as a biological threshold limit value for chronic exposure to mercury vapor. It must be noted that blood, hair and urine mercury levels reflect recent exposure and do not correlate with total body burden.

**Blood Hg**

The concentration of mercury in blood may be influenced by recent exposure and dietary habits, particularly the consumption of fish containing methyl mercury. Studies have demonstrated better correlations between blood mercury and mercury in air, than between urinary excretion of mercury and the prevalence of neuropsychomotor effects. Heavy metals should be considered as “systemic” toxicants. They have the potential to affect many organs and tissue. Failure in documenting history of exposure can lead to a delay in diagnosis as correlations between symptoms, and mercury concentrations in blood and urine are not well defined. It is important that a clinician collaborate with the laboratory to help understand all factors that influence mercury testing.

**REFERENCES**


**CONCLUSION**

Heavy metals should be considered as “systemic” toxicants. They have the potential to affect many organs and tissue. Failure in documenting history of exposure can lead to a delay in diagnosis as correlations between symptoms, and mercury concentrations in blood and urine are not well defined. It is important that a clinician collaborate with the laboratory to help understand all factors that influence mercury testing.

**Table 1. Practical aspects of biological monitoring of workers exposed to mercury**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Hg in blood</th>
<th>Hg in urine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confounding factors</td>
<td>Sample contamination, dental amalgam fillings, drugs, fish consumption, coal stove – fires.</td>
<td>Sample contamination, dental amalgam fillings, drugs</td>
</tr>
<tr>
<td>Half life</td>
<td>Fast phase – ±20 days</td>
<td>Slow phase – ±20 days</td>
</tr>
<tr>
<td>Reference: non-occupationally exposed individuals</td>
<td>&lt; 1 μg/dl</td>
<td>&lt; 5 μg/g creatinine</td>
</tr>
<tr>
<td>ACGIH-BEI</td>
<td>Inorganic 15 μg/L (ES, EW)</td>
<td>35 μg/g creatinine (PS)</td>
</tr>
<tr>
<td>DFG-BAT</td>
<td>Inorganic 25 μg/L (NC)</td>
<td>Organic 100 μg/L</td>
</tr>
</tbody>
</table>

**REFERENCES**