

# Mercury: A Review on the Target Organs and Toxic Effects

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## ABSTRACT

**Objective:** This paper aims to review the targets organs and toxicity upon exposure to Hg, the most toxic metal found on earth, via ingestion exposure pathway.

**Method:** The materials were accessed from online databases that cover topics such as mercury exposure and seafood consumption as well as mercury exposure and health effects among sensitive and general population.

**Result:** Mercury poisoning from ingestion exposure pathway are caused by both organic and inorganic mercury species as both are absorbed through the GIT. The prime target organ for inorganic mercury is the renal system whereas that of organic mercury is the central nervous system. Among adults, the reported health effects include nephritic syndrome, deficits of intelligence quotient, decrement in motor as well as attention performance and infertility. For children, numerous health effects were reported which includes impacts on cognitive thinking, memory, attention, language, fine motor skills and visual spatial skills, cerebral palsy-like symptoms, ASD, ADHD, cardiovascular as well as immunologic disorders

**Conclusion:** Both inorganic and organic mercury species are potential toxicant and neurobehavioral impairments are the prime outcome. Women at reproductive age, pregnant as well as lactating mothers, fetus and children are the groups most sensitive for mercury exposure and its toxic effects.

**Keywords:** *Mercury, Ingestion, Target organ, Toxicity*

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## 1. Introduction

Mercury (Hg) is a heavy metal that occurs naturally in the environment as well as from industrial activities and is a potential toxicant. The toxicity of Hg is dependent on the chemical form whereby the organic is more toxic than the

inorganic Hg. Elemental and inorganic Hg (IHg) from industrial waste settles onto sediment and aquatic environment where it is microbiologically transformed into the organic methylmercury (MeHg) through a process called methylation (Zahir et al., 2005). In aquatic environment, the MeHg along with IHg accumulates in aquatic organism such as fish, shellfish and mammals.

Methylmercury is the most toxic Hg compound and has a strong tendency to bio-accumulates in seafood and terrestrial animals that feed on seafood (Houserova et al., 2007). Due to the position at the top of food chain, human being are the group most affected by MeHg toxicity (WHO, 2008; Zahir et al., 2005). In addition, IHg exposure from seafood intake is also of great concern as almost 8-15% of IHg will be absorbed in the gastrointestinal tract (GIT) (Cheng et al., 2009; WHO, 2008; Ohno et al., 2007).

Scientists are worried about the rising toxicity of Hg as there are increasing concentrations of Hg in the air, sediment, water and eventually in aquatic organism. Mercury absorbed into the gastrointestinal tract enters the bloodstream and distributed to other bodyparts to exert toxic effect. This paper was attempted to review the target organs and various toxicity of Hg exposed from ingestion exposure route to different population groups.

## 2. Materials and Method

The materials for this review paper were accessed from online databases such as Science Direct, PubMed and Scopus. All of the references used were journal articles written in English language, published within 1994 to 2015, emphasizing on toxic effects due to Hg exposure.

The keywords used to search articles were “mercury exposure”, “methylmercury exposure”, “total mercury exposure”, “seafood intake AND mercury exposure”, “mercury exposure AND target organ” and “mercury exposure AND toxic effect”. Besides that, a comprehensive search was conducted which focused on the articles related to the association between fish consumption and Hg exposure among sensitive groups and the health effects

## 3. Results

Mercury is considered as a systemic toxicant due to its capability of inducing multiple organ damage even at low exposure level (Tchounwou et al., 2012). Mercury poisoning from ingestion are caused by both organic and inorganic forms as both the species are absorbed through the GIT. Health impacts following Hg exposure may vary between genders and for different age groups of the population.

### 3.1. Adults

Among adults, health impact owe to Hg exposure via ingestion route is caused by IHg and demethylation of organic MeHg to Hg<sup>2+</sup>.

Approximately 7% to 15% of doses of IHg salts, are absorbed in the gastrointestinal tract after ingestion (Liu et al., 2008). The highest concentration of IHg is found in the kidney, which is a major target organ of IHg. About 1 to 4 g of mercuric chloride, a form of IHg salt is fatal in adults (Von Burg, 1995). Besides, an acute high dose exposure to IHg salts causes severe gastrointestinal symptoms due to extensive corrosive damage to the GIT. Following this are symptoms and signs of mercurial stomatitis and impaired kidney function.

The target organ toxicity of inorganic mercury is kidney damage, mainly in the proximal convoluted tubules (Park and Zheng, 2012). The clinical manifestations includes polyuria and proteinuria which may led to nephritic syndrome in severe cases, with hematuria and anuria (WHO 1991 and Clarkson & Magos, 2006). These effects may vary with their co-occurrence with other heavy metals (Polak-Juszczak, 2015). For instance, selenium (Se), to which Hg binds to form complexes such as selenoprotein [(HgeSe)<sub>n</sub>]<sub>m</sub> and Hg selenide (HgSe), a simple, but stable compound, may well reduce the Hg toxicity (Polak-Juszczak, 2015).

Langford and Ferner (1999) stated that organic MeHg, are important cause of poisoning in which the toxicity may be delayed for weeks to months, with predominant GIT and CNS effects (Morisset et al., 2013). Methylmercury is lipophilic in nature and distributes throughout the body, preferentially stored in the brain and CNS (Philbert et al., 2000) to express serious adverse effects on the development and functioning of CNS (Salehi et al., 2010). It was estimated that about 5% of dietary MeHg is found in the blood and doubled (10%) in the brain (Castoldi et al., 2003; Salehi et al., 2010) and about 5% of adults exposed to the MeHg would experience neurological impairments to a certain extent (WHO, 2008).

The renowned adverse neurological impairment of Hg on human health include the subtle syndromes such as deficits of intelligence quotient and decrement in motor as well as attention performance (Faial et al., 2015). For instance, adults with hair THg below 50µg/g in Amazon demonstrated near visual contrast sensitivity, decreased manual dexterity, tendency for increased muscular fatigue and decreased muscular strength (Zahir et al., 2005). In Tanzania, the fish consumers with hair THg levels <10ppm have demonstrated a very high rate of sensory disturbance such as glove and stocking type (Harada et al., 1999). Yokoo et al. (2003) studied male and female residing in villages on the Cuiaba River, Brazil and found a mean hair Hg of 4.2 ± 2.4µg/g. Even with low exposure level, the respondents demonstrated disruption of attention, fine motor function and verbal

memory which associated with fish consumption and hair Hg levels (Yokoo et al., 2003).

Despite being a neurotoxicant, MeHg is also a reproductive toxicant. Women would be unable to conceive in the event of high MeHg exposure or else the pregnancy rate is low or the fetus is aborted or is stillborn. Abnormal pregnancy such as stillbirth and spontaneous abortion was found significantly in Minamata during 1950s and 1960s due to widespread MeHg poisoning in the city (Itai et al., 2003). Another study was conducted among Hong Kong males that consume fish or shellfish four or more times a week averaging about 60 kg of fish per year. It was deduced that eating Hg contaminated fish steadily for many years suggests a daily mercury intake of only 0.3 to 0.7 mg/kg bw is sufficient to inhibit spermatogenesis (Dickman and Leung, 1998)..

### 3.2. Fetus, Infants and Children

Being a teratogen, Hg can have serious adverse effects during prenatal exposure (Salehi et al., 2010). Studies have discovered adverse neurodevelopmental outcomes including microcephaly, seizures, and mental retardation associated with consumption of fish and bread highly contaminated with MeHg (Yau et al., 2014). Sex ratio of offspring showed a decrease in male child birth in fishing communities of Minamata in the 1950s and 1960s due to increase in male stillbirth which reflects that male fetus are more susceptible (Sakamoto et al., 2001).

Both MeHg and IHg ingested by mothers can pass through the placenta (Yau et al., 2014; Ask et al., 2002; Goldman and Shannon, 2001). A distinctive attention was given to MeHg as it readily crosses the blood–brain barriers of fetus following placental transfer to exert toxic effect on brain development (Salehi et al., 2010; Sakamoto et al., 2008; Ramirez et al., 2000). To make it worse, MeHg accumulates in the fetus at higher concentrations compared to the mother (Yau et al., 2014; Ni et al., 2011; Savabieasfahani et al., 2012).

In children, negative impacts on cognitive thinking, memory, attention, language, fine motor skills, and visual spatial skills have been seen in those exposed to MeHg in the womb (Freire et al., 2010; Oken et al., 2008a; Baneerji et al., 2007; Evans, 2006; Roegge et al., 2006). It was found that among pregnant women exposed to low level of MeHg who displayed mild or zero manifestations of Hg poisoning, the infants had severe cerebral palsy-like symptoms (Li et al., 2010). At a higher exposure level, for instance, among women with maternal hair Hg between 10–20 µg/g, decreased motor function and memory has been reported in their children (Grandjean et al., 1998).

Methylmercury is also a potential contributor to autism spectrum disorder (ASD) (Yau et al., 2014). A study has

been done to examine the association between prenatal Hg exposure and risk of ASD by direct measurement of total Hg in blood collected prior to the diagnosis of ASD. Mercury levels were elevated in the new born population compared to maternal samples. In another retrospective study, mean blood Hg levels were 1.9-fold significantly increased among children diagnosed with an ASD (21.4 µg/L) in comparison to controls (11.4 µg/L) ( $P < 0.0001$ ) (Geier et al., 2010).

Likewise, a study among children with attention-deficit hyperactivity disorder (ADHD), another common neurobehavioral disorder, showed a significant difference in blood Hg levels compared to that of controls, (geometric mean 18.2 nmol/L [95% CI 15.4 – 21.5 nmol/L] vs. 11.6 nmol/L [95% CI 9.9 – 13.7 nmol/L],  $p < 0.001$ ). Also blood Hg level above 29nmol/L had 9.69 times (95% CI 2.57 – 36.5) higher risk of having ADHD after adjustment for confounding variables; age, gender and parental occupational status (Cheuk and Wong, 2006).

Other effects have been associated with early exposure too such as cardiovascular and immunologic disorders (Karagas et al., 2012; Chan and Egeland, 2004). The development of cardiovascular homeostasis is affected following prenatal exposure to MeHg. This has caused the systolic and diastolic blood pressure to increase 13.9 mmHg when cord blood Hg level increase from 1 to 10µg/l (Sorensen and Murata, 1999).

## 4. Discussion

From the extended list of toxic effects, fetus, infants and children are clear high-risk groups for MeHg exposure due to the vulnerability of the developing brains (Sakamoto et al., 2008) which has resulted in extreme fetal neurotoxicity ever since Minamata Disease, 1956 (Castano et al., 2015). This is also due to typical behaviour (such as hand to mouth activity, outside activities, breastfeeding) and physiological differences (such as body weight, inhalation rates) (Morisset et al., 2013).

## 5. Conclusion

Nevertheless, women at reproductive age are the prime route for fetal exposure and are another at risk group (Sakamoto et al., 2008; ATSDR, 1999). The toxic MeHg is effectively absorbed from the GIT and readily crosses the placenta of pregnant mothers as well as breast milk of lactating mothers (WHO, 2008) posing threat for their descendants. On the other hand, women exposed to IHg are at risk of CNS and GIT negative effects too to a certain extent as well as kidney damages which may indirectly influence their well-being and reproduction.

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