Journal of Hazardous Materials 306 (2016) 376–385

Contents lists available at ScienceDirect

Journal of Hazardous Materials

journal homepage: www.elsevier.com/locate/jhazmat

Review

# A review on the distribution of Hg in the environment and its human health impacts

Ki-Hyun Kim [a,*], Ehsanul Kabir [b], Shamin Ara Jahan [c]

[a] Dept. of Civil and Environmental Engineering, Hanyang University, Seoul 133-791, Republic of Korea
[b] Dept. of Farm, Power & Machinery, Bangladesh Agricultural University, Mymensingh, Bangladesh
[c] BRAC Clinic, Dhaka, Bangladesh

## HIGHLIGHTS

- Exposure to high or low levels of Hg has been reported to cause various illness of human.
- The adverse health effects of Hg are affected by the speciation of Hg accumulated in the body.
- The current understanding of mercury exposure, health effects, and risk assessment is reviewed.

## ARTICLE INFO

*Article history:*
Received 17 July 2015
Received in revised form 8 November 2015
Accepted 17 November 2015
Available online 21 November 2015

*Keywords:*
Mercury exposure
Speciation
Occupational risk
Health effects

## ABSTRACT

Exposure to mercury is a silent threat to the environment and human life. It has the potential to harm almost every organ and body system. Mercury compounds are classified in different chemical types such as elemental, inorganic, and organic forms. The most significant source of ingestion-related mercury exposure in humans and animals is the consumption of fish. Long-term exposure to mercury compounds from different sources (e.g., water, food, soil, and air) can lead to toxic effects on skin, cardiovascular, pulmonary, urinary, gastrointestinal, and neurological systems. Mercury toxicity is found to pose more significant health hazards to certain occupational groups (e.g., goldminers and dental personnel). Because continuous exposure to mercury can be dangerous, it is desirable to re-evaluate the current reference (risk-free) values. This paper reviews the route of Hg exposure to humans, its human health impacts, the associated risk assessment, and treatment based on the recent findings from various studies.



**Contents**



* Corresponding author.
*E-mail addresses:* kkim61@nate.com, kkim61@hanyang.ac.kr (K.-H. Kim).

http://dx.doi.org/10.1016/j.jhazmat.2015.11.031
0304-3894/

## 1. Introduction

Mercury (Hg) has received special attention because of its potential to cause adverse effects on human health and the environment throughout the world. The toxic effects of mercury imposed on humans and other organisms are dependent on many factors including the chemical form, the amount, the exposure pathway, and differences in vulnerability between exposed subjects [1,2]. Human exposure to mercury may occur via a variety of pathways including consumption of foodstuffs (e.g., fish), occupational and household uses, dental amalgams, and mercury-containing vaccines [3].

Human activity is the main cause of mercury releases, particularly coal fired power stations, residential coal burning for heating and cooking, industrial processes, waste incinerators, and mining activities for gold and other metals [4]. Mercury also occurs naturally and is found in air, water, and soil. It is also released into the environment from various natural sources such as volcanic activity, weathering of rocks, geologic deposits of mercury, and volatilization from the ocean [4,5]. The occurrence of cataclysmic volcanoes through which excessive quantities of volatile mercury are injected into the stratosphere has the great potential to alter its global and regional cycle [5]. Although all types of natural media (rocks, sediments, water, and soils) contain small but varying amounts of mercury, scientists have also found some mineral and thermal springs that are naturally enriched in mercury [6].

The adverse health effects of Hg are the result of the speciation of Hg accumulated in the body, the extent of exposure (quantity, frequency, and duration) and the age of the subject [7]. In aquatic environments, inorganic mercury is microbiologically transformed into a lipophilic organic compound (methylmercury) that makes it more prone to biomagnification in food chains [8]. Consequently, populations with traditionally high dietary intake of seafood should be subject to one of the most effective routes of explosure [9]. Mercury has also been found to be a causative agent for various disorders (e.g., neurological, nephrological, immunological, cardiac, motor, reproductive, and even genetic problems) [2]. Exposure to high levels of Hg has been reported to harm the brain, heart, kidneys, lungs, and immune system indicated by a number of symptoms (e.g., tremors, emotional changes, insomnia, weakness, muscle atrophy, twitching, headaches, disturbances in sensations, changes in nerve responses, and performance deficits on tests of cognitive function) [10].

In view of the numerous recent reports dealing with mercury toxicity, environmental contamination should be checked and evaluated more thoroughly. Therefore, accurate information regarding the threat of mercury exposure is critical. In this regard, this paper reviews the existing literature, highlights current understanding, and identifies issues about mercury exposure, health effects, and risk assessment.

## 2. Mercury in various media

### 2.1. Hg in air

Background atmospheric concentrations of Hg typically range from 1.3 to 1.7 ng $m^{-3}$ in the Northern Hemisphere and from 1.1 to 1.3 ng $m^{-3}$ in the Southern Hemisphere [11]. On a global scale, the net atmospheric Hg deposition is determined by the overall emissions, whereas deposition at the local scale is controlled by atmospheric processes and the speciation of regional and local emissions. It is estimated that the annual global emissions of Hg (to the atmosphere) range from 6500 to 8200 Mg $year^{-1}$ [12]. The concentration levels of Hg in the atmospheric environment are shown in Table 1 A.

Although mercury is not classified as one of the six criteria air pollutants, the EPA still regards mercury as a harmful air pollutant [13]. The atmosphere is the foremost transport pathway of Hg emissions, contributing to the redistribution of Hg in terrestrial, freshwater, and marine ecosystems [14]. As Hg is stable with a relatively long residence time (e.g., several months to a year), it can be transported long distances before dry or wet deposition [11]. Although the emission of mercury is sensitive to temperature, its spatial distribution is also controlled by meteorological conditions (wind direction and velocity) [15]. Mercury produced by man-made sources can therefore be transported to remote locations such as the Arctic and Antarctic [16].

The chemical reactions and the partitioning of mercury in gas and aqueous phases are critical components to assess its atmospheric residence time [17]. Boening [18] suggested that environmental variables such as pH, redox potential, water chemical composition, soil type, and geology affect the environmental cycling of Hg through sorptive removal or other reactions. A large portion of the mercury present in the atmosphere today is the result of many years of releases mainly due to anthropogenic activities. Primary sources, both natural and of anthropogenic origin, transfer Hg from long-lived lithosphere reservoirs to the atmosphere [19]. This Hg deposits to land and oceans. One of thr re-emission of deposited Hg represents significant secondary sources that exchange Hg among different surface environmental reservoirs using the atmosphere as a vehicle [19]. Primary sources increase the global pool of Hg in surface reservoirs, while secondary sources redistribute it among and within ecosystems.

### 2.2. Hg in water

There are a number of ways through which mercury participates in its cycling in the aquatic systems. Rain and snow can carry mercury from the air into surface waters such as lakes, rivers, and oceans. Mercury can seep into underground water supplies from industrial and hazardous waste sites. Past applications of mercury-based pesticides on agricultural lands (such as farms and fruit orchards) can also be mobilized to transfer Hg into nearby surface waters or underground water supplies through soil layers. Bacteria in lakes, streams, and ocean sediments then convert Hg from elemental into organic form compounds such as methylmercury [20,21].

The mercury concentration levels in water of different sources are listed in Table 1B. In Nanjing, China, Zhu et al. [22] found that the volume-weighted mean (VWM) concentration of mercury in rainwater was 52.9 ng $L^{-1}$ (range: 46.3–63.6 ng $L^{-1}$). In México, mercury dissolved in the drinking water was seen at a range of 10–170 ng $L^{-1}$ [17]. In Denmark, Grandjean [23] found mercury concentrations in drinking water from 5 to 100 ng $L^{-1}$. In Poznań, Poland, mercury was found as $20 \pm 8$ ng $L^{-1}$ (range 8–40) in surface waters (ponds, lakes, streams, and rivers), while its content in ground water was $1.3 \pm 0.7$ ng $L^{-1}$ (range 0.8–4.1) [24]. Mercury concentrations of the Boise and Snake rivers, USA, ranged from 0.73 to 1.21 ng $L^{-1}$, while that in the Brownlee reservoir was moderately high at 8.78 ng $L^{-1}$ [25].

**Table 1**
Mean concentration of mercury in various environmental media.

A. Air

| Order | Location | Study period | Concentration ($ng\,m^{-3}$) | Reference |
|---|---|---|---|---|
| 1 | Windsor, ON, Canada | 2007–2011 | 0.56–4.93 | [117] |
| 2 | Northern Hemisphere | 2003–2008 | 0.71–3.82 | [11] |
| 3 | Southern Hemisphere | 2003–2008 | 0.37–3.97 | [11] |
| 4 | Alberta, Canada | 2010–2013 | 0.54–6.43 | [118] |
| 5 | South China | 2008–2009 | 1.12–8.68 | [119] |
| 6 | Northeast China | 2005–2006 | 1.28–9.49 | [120] |
| 7 | An-Myun Island, Korea | 2004–2006 | 0.10–25.4 | [121] |

B. Water

| Order | Medium | Location | Study period | Concentration ($ng\,L^{-1}$) | Reference |
|---|---|---|---|---|---|
| 1 | Rainwater | Nanjing, China | 2011–2012 | 46.3–63.6 | [22] |
| 2 | Drinking | Mexico | 2007 | 10–170 | [17] |
| 3 | water | Denmark | 2006–2007 | 5–100 | [23] |
| 4 | Surface waters | Poznań, | 2003–2004 | 8–40 | [24] |
| 5 | Ground water | Poland | | 0.8–4.1 | |
| 6 | River water | USA | 2013 | 0.73–1.21 | [25] |
| 7 | Reservoir water | | | 8.78 | |
| 8 | Stream | Idrija, Slovenia | 1998–2000 | 2.8–322 | [26] |
| 9 | water | Guizhou, China | 2004 | 22–360 | [27] |
| 10 | | Almaden, Spain | 1998–2001 | 7.6–20300 | [28] |

C. Soil

| Order | Location | Site type | Study period | Concentration ($\mu g\,g^{-1}$) | Reference |
|---|---|---|---|---|---|
| 1 | Texas, USA | Hg mine | 2012 | 3.8–11 | [34] |
| 2 | Santo, Brazil | Mangrove areas | 1996–1997 | 0.04–1.19 | [36] |
| 3 | Wanshan, China | Hg mine and smelting | 2006–2007 | 15–119 | [32] |
| 4 | Qingzhen, China | Coal fired power plant and other industries | | 0.20–1.70 | [32] |
| 5 | Poznań, | Floodplain soil | 2004 | 0.75–8.84 | [33] |
| 6 | Poland | City area | 2004 | 0.72–3.03 | [33] |
| 7 | Tarkwa, Ghana | Mining communities | 2006 | 0.22–0.59 | [35] |

The presence of considerably high concentrations of Hg exceeding the common criteria by several times or more has been found commonly in stream waters in polluted areas. For instance, significantly high and variable levels of Hg were found in a number of locations surrounding abandoned cinnabar mines: 2.8–322 $ng\,L^{-1}$ (Idrija, Slovenia [26]), 22–360 $ng\,L^{-1}$ (Guizhou, China [27]), and 7.6–20300 $ng\,L^{-1}$ (Almaden, Spain [28]). The US EPA has set the maximum contaminant guidance levels for Hg in drinking water to 2000 $ng\,L^{-1}$ or that of the aquatic life criteria as 1400 $ng\,L^{-1}$ (acute exposure) and 770 $ng\,L^{-1}$ (chronic exposure) [13].

### 2.3. Hg in soil and plants

The dynamic between the amount of Hg that exists in the soil and its uptake by plants is not linear, as it is affected by the combined effects of several variables (e.g., the cation-exchange capacity, soil pH, soil aeration, and plant species) [29,30]. In addition, its accumulation in a plant body is also controlled by such variables as their species and/or the variety [31].

A summary of mercury concentration levels in soil layers around the globe is shown in Table 1C. High levels of Hg (range: 15–119 and median: 25 $\mu g\,g^{-1}$) were found in soil near mercury mining and smelting in Wanshan, China [32]. In contrast, near a coal fired power plant and other industries in Qingzhen, China, Hg concentrations in soil were recorded as 0.2–1.7 (median 0.3) $\mu g\,g^{-1}$ [32]. Mercury concentrations in the floodplain soil samples of the Warta river, Poznań, Poland were found to be 0.75–8.84 (median 3) $\mu g\,g^{-1}$ and from the city area 0.72–3.03 (median 1.83) $\mu g\,g^{-1}$ [33]. Considerably elevated levels of Hg (3.8–11 $\mu g\,g^{-1}$) were observed from soil samples collected within 300 m of an inactive Hg mine in the Big Bend area, Texas, USA relative to samples of baseline sites (0.03–0.05 $\mu g\,g^{-1}$) [34].

Moderately reduced levels of soil Hg were also observed in many other studies, although most of these appeared to be influenced by less noticeable source processes. Hayford et al. [35] found Hg concentration in soil samples in the range of 0.22–0.59 $\mu g\,g^{-1}$ from the mining communities in and around Tarkwa in the Western Region of Ghana. Hortellani et al. [36] analyzed 31 sediment samples collected from mangrove areas under the influence of urban, industrial, and harbor related sources in Santo, Brazil. The range of the soil Hg values was found to be between 0.04 and 1.19 $\mu g\,g^{-1}$. About 35% of these samples showed Hg content surpassing 0.70 $\mu g\,g^{-1}$, which is the probable level to cause adverse effects on the biological community [37]. A line of evidence indicates that mercury is responsible for reduction of micro-biological activity vital to the terrestrial food chain in soils [38,39]. Preliminary critical limits to prevent ecological effects due to mercury accumulated in organic soils are recommended as 0.07–0.3 $\mu g\,g^{-1}$ for the total mercury content in soil [40].

Concentration of Hg in plants reflects the environmental exposure of Hg and ecological niches. A widespread increase in the atmospheric deposition of Hg may result in increases in Hg levels in plant tissues, which in turn may contribute to the elevated bioaccumulation of Hg. Most of the plants that uptake Hg tend to accumulate it in the roots and even in the shoots, either due to translocation or direct absorption of the vapor form [41]. Some plants (such as corn, wheat, and peas) have very low levels of mercury, even if grown in soils with significantly high levels of Hg relative to the background area. Mushrooms, however, can accumulate high levels of Hg if grown in contaminated soils. It has been reported that the concentration of mercury in rice grains can reach up to 569 $g\,kg^{-1}$ [42]. Mercury concentrations in wheat and rye grains, nine varieties of vegetables, and seven varieties of fruit averaged $2.4 \pm 2.3$, $0.5 \pm 0.4$, and $1.1 \pm 0.9$ $\mu g\,kg^{-1}$, respectively [43].

Dunagan et al. [44] found mercury concentrations of 0.033 and 0.004 ppm in spinach and wheat flour samples, respectively. The mean value of mercury from approximately 100 species of tropical plants was 0.015 ppm where the mercury levels in deciduous trees and herbaceous plants were 0.028 and 0.017 ppm, respectively [45]. In Tarkwa, Ghana, Hg concentrations in cassava and plantain were found to be 0.22–0.59 and 0.19–0.52 $\mu g\,g^{-1}$, respectively [35].

### 2.4. Hg in fish

Traces of mercury have been measured in a wide variety of foods including dairy products, meats, poultry, eggs, pasta, fruits, and vegetables. However, the levels of mercury in these foods are very low compared to the levels found in fish [2]. In terms of relative significance, the contribution of common foods is generally not as important as fish. The most common source of human exposure to methylmercury is in fact accounted for by the consumption of certain types of fish [46].

Methylmercury is produced by anaerobic organisms, largely bacteria, which reside in the deep, oxygen-deficient, benthic regions, is identified as a significant threat to human health [47]. Traces of mercury, largely in the form of methylmercury, can be found in nearly all fish species, although its levels are higher in some fish types than in others (Table 2). Fish bioaccumulate methylmercury in their muscle tissues, primarily through consumption of organisms that contain methylmercury [48]. The biomagnification of methylmercury proceeds through the food chain, when predators (such as piscivorous fish) eat what has already been bioaccumulated in their muscle tissues. Methyl mercury is typically ingested by fish and bioaccumulates in both the tissues of fish and the humans that eat these fish.

Over time, top predator fishes (e.g., sharks and swordfish) that regularly consume prey with relatively high levels of methylmercury will maintain it at much enhanced levels in their tissue relative to either their prey or the surrounding environment. Large predatory fish can hence contain as much as 100,000 times more methyl mercury than the surrounding water medium. This can cause damage to the nervous system as well as the teratogenesis of humans who consume such fish [49].

It was reported that bighead carp gathered more mercury than grass carp, as the former consumed large amounts of small plankton and sucked up sediments that contained a sizable amount of methylmercury [50]. For most people, the risk of mercury by eating fish and shellfish is not a health concern. However, some of them contain considerably high levels of mercury that can harm an unborn baby or young child's developing nervous system. Therefore, the Food and Drug Administration (FDA) [46] and the Environmental Protection Agency (EPA) [13] are advising pregnant women or women who may become pregnant, nursing mothers, and young children to eat fish and shellfish that are lower in mercury and to avoid some types of fish.

Mercury concentrations in individual fish tissue samples collected from the Boise and Snake rivers, USA, ranged from 0.14 to 0.38 ppm [25]. They found that methylmercury concentrations in fish collected from the Brownlee Reservoir ($0.32\,mg\,kg^{-1}$) and the Boise River ($0.33\,mg\,kg^{-1}$) exceeded the human health criteria of methylmercury (0.3 ppm or $mg\,kg^{-1}$) set by the state of Idaho in the USA. In New Jersey, USA, levels of mercury above 0.5 ppm were found, a level of human health concern for those who consume fish regularly [48]. Likewise, 48.8% of the sampled population of 36,422 lakes in the USA had mercury tissue concentrations that exceeded 0.3 ppm [51]. Surprisingly, mercury concentration as high as 2.2 ppm was also found in Anglerfish off the coast of Italy [47].

## 3. Sources of Hg as the route of human exposure

Mercury exists in several forms such as elemental (or metallic), inorganic, and organic compounds in all types of environmental media [6]. It is a naturally occurring element that cannot be created or destroyed. However, because of distortion induced by human activities, its cycling is governed by both anthropogenic and natural processes. About 7500 t of mercury are emitted into the atmosphere each year [14]. Fig. 1 compiles this amount by source and the emission inventory of Hg in various locations around the globe.

Metallic mercury is used in a variety of household, industrial, and medical products (including thermostats, fluorescent light bulbs, barometers, glass thermometers, and some blood pressure devices). As the mercury in these devices is contained in a glass or metal frame, its presence does not generally pose a risk unless damaged or broken. However, one can be exposed to metallic mercury vapors if the inflow of air is affected by strong source process, e.g. hazardous waste sites, waste incinerators, or power plants that burn mercury containing coal or other fossil fuels [6]. More specifically, exposure to mercury compounds is much more likely to occur at hazardous waste sites via contact with contaminated surface soil, drinking well water, or eating fish from contaminated water [28].

## 4. Occupational risk of Hg exposure

Another significant route to Hg exposure is occupational contact. Occupations that have great potential for mercury exposure include manufacturers of electrical equipment or automotive parts, chemical processing plants, metal processing, construction and building materials (e.g., electrical switches and thermometers), and the medical professions (medical, dental, and other health services) [52]. Family members of these workers exposed to mercury may also be subject to re-exposure depending on the situation.

Dental offices are known to be one of the largest users of inorganic mercury. It is well documented that dentists and dental personnel working with amalgam are chronically exposed to mercury vapour, which accumulates in their bodies at much higher levels than those of other occupations. Elemental mercury is a key ingredient in dental amalgam used as a filling material. Despite the availability of other mercury-free options, dental amalgams continue to be used worldwide because of favorable cost, familiarity, ease of use, and durability [53].

Dentists, dental assistants, technicians, and other workers in odontology or dental settings are exposed to mercury from amalgam related tasks and workplace conditions including bulk storage, preparation of amalgam, finishing and polishing the amalgam surface, restoration of old fillings, and cleanup of work areas and tools [54,55]. The mean Hg concentration from a personal dosimeter in the dentist's breathing zone was found to be $29.2\,\mu g\,m^{-3}$, which is higher than the Occupational Exposure Standard (OES) ($25\,\mu g\,m^{-3}$) [56]. Likewise, urinary mercury levels of dentists (3.1 nmol Hg/mmol creatinine) were found to be higher by 3–4 times those of control subjects (0.99 nmol Hg/mmol creatinine) [57].

Drake et al. [58] recorded the 8-h time-weighted average (TWA) of airborne mercury exposure concentrations of $183\,\mu g\,m^{-3}$ (range: 0.1–$6315\,\mu g\,m^{-3}$) in workers' breathing zones at gold mines in Venezuela. They found that 20% of the TWA airborne mercury exposure measurements were above the NIOSH recommended exposure limit (REL) of $50\,\mu g\,m^{-3}$, while 26% exceeded the American Conference of Governmental Industrial Hygienists (ACGIH) threshold limit value (TLV) of $25\,\mu g\,m^{-3}$. Workers at a fluorescence bulb factory in Iran were found to be exposed at much higher levels of Hg ($650\,\mu g\,m^{-3}$) than those of a compact fluorescent bulb factory ($<10\,\mu g\,mg\,m^{-3}$).

**Table 2**
Summary of mercury levels in fish.

| Order | Species | Place | Period | Mean concentration (ppm) | Reference |
|---|---|---|---|---|---|
| 1 | Swordfish | USA | 1990–2010 | 0.99 | [122] |
| | | Canada | 2002–2004 | 0.85 | [123] |
| | | Canada | 2002 | 1.82 | [49] |
| | | Pakistan | 2004 | 0.97 | [2] |
| 2 | Shark | USA | 1990–2007 | 0.98 | [113] |
| | | Canada | 2002 | 1.36 | [49] |
| | | Pakistan | 2004 | 0.99 | [2] |
| 3 | Tuna | USA | 1991–2010 | 0.39 | [113] |
| | | Canada | 2002–2004 | 0.37 | [114] |
| | | Canada | 2002 | 0.93 | [49] |
| | | Pakistan | 2004 | 0.38 | [2] |
| 4 | Tuna (bigeye) | USA | 1991–2005 | 0.69 | [113] |
| | | Canada | 2002–2004 | 0.65 | [114] |
| 5 | Tuna (albacore) | USA | 1992–2008 | 0.36 | [113] |
| | | Canada | 2002–2004 | 0.34 | [114] |
| 6 | Tuna (yellowfin) | Canada | 2002 | 0.26 | [49] |
| | | USA | 1992–2009 | 0.35 | [113] |
| 7 | Tilefish (Gulf of Mexico) | USA | 1992–2008 | 1.45 | [113] |
| 8 | Tilefish (Atlantic) | USA | 1992–2008 | 0.144 | [113] |

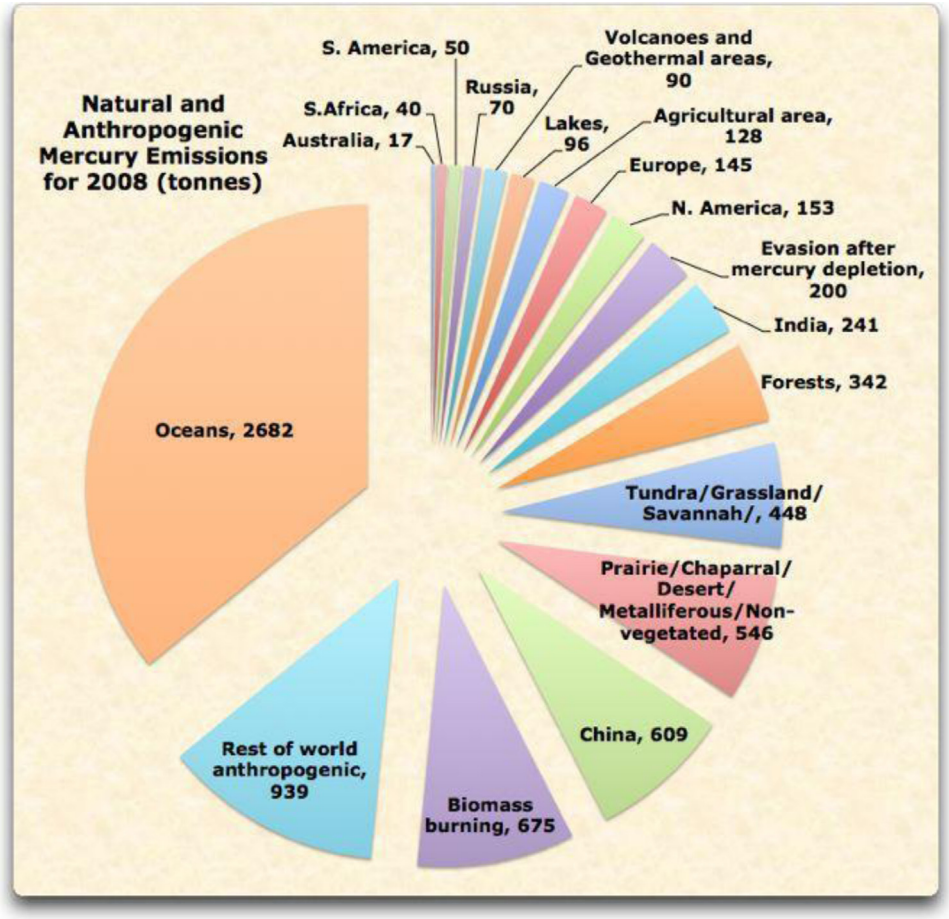


**Fig. 1.** Natural and anthropogenic sources of atmospheric mercury emissions (source: [14]).

In a fluorescent lamp factory in Egypt, a group of people exposed to Hg had significantly high contents of urinary Hg ($44.1 \pm 17.5\ \mu g\text{-}g^{-1}$ creatinine$^{-1}$) relative to a control group ($6.1 \pm 4.9\ \mu g\text{-}g^{-1}$ creatinine$^{-1}$) [59]. Mercury levels for hair, urine, toenails, and blood averaged at least 2 times higher for dental personnel than for their control group. A Lebanese study found that 25.25% of dentists had hair mercury levels over 5 ppm, while 7.07% of them had levels over 10 ppm [60]. A US national sample of dentists provided by the American Dental Association had an average of $5.2\ \mu g\ L^{-1}$. If extended to a large sample of dentists, 10% of them had urinary mercury levels over $10.4\ \mu g\ L^{-1}$. Note that the top 1% of them had Hg levels over $33.4\ \mu g\ L^{-1}$, indicating daily exposure

levels exceeding 100 μg. In another large scale study conducted in the USA, the average level of urinary Hg among dentists was found at 3.2 μg $L^{-1}$ [53].

## 5. Health effects of Hg exposure

The human toxicity of Hg varies with such variables as its chemical form, dose, and rate of exposure. Through consumption of mercury in food and environmental exposure, human beings have been confronted with the insidious and debilitating nature of mercury poisoning [61].

A number of diseases including central nervous system defects and erethism as well as arrhythmias, cardiomyopathy, and kidney damage are suspected to be associated with mercury exposure [62]. Necrotizing bronchitis and pneumonitis arising from inhalation of mercury vapor have also been suggested to cause in respiratory failure [61]. Mercury is also considered a potent immunostimulant and suppressant depending on exposure dose and individual susceptibility, producing a number of pathologic sequelae including lymphoproliferation, hypergammaglobulinemia, and total systemic hyper and hyporeactivities [63]. A plot chart to briefly classify the health effects induced by mercury exposure is depicted in Fig. 2. Discussions covering each of these components are provided below.

### 5.1. Neurological effects of Hg

Neurological disorders are among the most common and serious problems caused by mercury, which include, but are not limited to, memory loss, moodiness, depression, anger, and sudden bursts of anger/rage/violence, self-effacement, suicidal thoughts, and lack of strength to resolve anxiety or resist obsessions or compulsions [52,64,65].

Many studies of neurological diseases have found evidence that amalgam fillings may play a major role in the development of conditions such as depression, schizophrenia, bipolar disorder, and memory problems [7,66,67,68]. Accordingly, long-term exposure to chronic low doses of mercury has also been found to cause various conditions such as neurological diseases, sleeping disorders, hearing loss, and mood problems [67,69]. Neurological effects have thus been documented at the very low levels of exposure (urine inorganic Hg < 4 μg $L^{-1}$) that are commonly experienced by those with amalgam fillings [70].

Mercury has been found to cause memory loss by deactivating enzymes necessary for the production of brain cell energy and proper assembly of the protein tubulin into microtubules [71]. Mercury is reported as being neurotoxic, as it can impact humans in several ways: to kill or damage brain cells and nerve cells; to generate high levels of reactive oxygen species (ROS) and oxidative stress; and to kill or inhibit the production of brain tubulin cells [72,73].

A study conducted at the US CDC found statistically significant associations between certain neurologic (developmental) disorders such as attention deficit disorder (ADD) and autism with exposure to mercury from vaccines containing thimerosal [74]. However, studies making such claims have been largely discredited. On the basis of a large epidemiological study, dental amalgam surfaces were also found to be highly correlated with epilepsy, migraines, mental disorders, diseases of the nervous system, disorders of the thyroid gland, cancer, and infectious diseases [75]. Mercury induced lipid peroxidation has been found to be a major factor in neurotoxicity along with decreased levels of glutathione peroxidation and superoxide dismustase (SOD) [76]. According to a prenatal exposure test of mercury vapor on newborn rat brains, decreases in nerve growth factor and other effects were observed only in 4 ppb levels [77]. However, such level are not much different from those with several amalgam fillings or other exposures.

Mercury can also cause depression and mood disorders through increased neurological problems in association with reductions in neurotransmitters dopamine, serotonin, noreprenephrine, and acetylcholinesterase [7]. In such cases, mercury has been found to accumulate and to affect the function of the brain limbic system [78]. Nylander et al. [79] found that the pituitary glands of a group of dentists had 800 times more mercury than controls. This may explain the higher levels of certain diseases (emotional problems, depression, suicide, etc.) among dentists [54]. High levels of methylmercury in the bloodstream of unborn babies and young children are suspected to harm the developing nervous system, depriving the child's capacity to think and learn to a degree [80]. Similarly, disruption of attention and verbal memory was also found in adults [81].

### 5.2. Renal effects of Hg

In humans and other mammals, the kidneys are the primary targets where mercuric ions accumulate after exposure to elemental or inorganic forms of mercury [82]. With organic mercuric compounds, multiple exposures to relatively large doses are generally required to induce renal injury [67]. Within the kidney, the pars rectum of the proximal tubule is the most vulnerable segment of the nephron to the toxic effects of mercury [83]. The principal target of mercury in the kidney is the proximal tubule and particularly the straight portion of the proximal tubule, called the pars recta or S3 segment [84].

Renal effects in humans have been observed after acute oral exposure to inorganic mercury [85]. Renal uptake and accumulation of mercury in vivo can proceed very rapidly. As much as 50% of a low dose of exposure to inorganic mercury (0.5 μmol $kg^{-1}$) has been shown to be confirmed from the kidneys of rats within a few hours [86]. Long-term (e.g., at or above 4 weeks) oral administration of mercury sulfide in mice increased the renal mercury burden, while decreasing circulating thyroxin ($T_4$) levels [87]. However, no data on nephrotoxicity were reported from this study.

### 5.3. Cardiovascular effects

Evidence shows that subjects exposed to toxic levels of Hg exhibited an increased occurrence of rapid heartbeat, irregular pulse, chest pains, heart palpitations, and high blood pressure [88]. The earliest widespread indications of the cardiovascular effects of mercury were seen in victims diagnosed with Acrodynia, primarily in children exposed to various mercury compounds. The cause of the disease was suspected to be a mercurous chloride compound called Calomel, which was commonly used as a teething powder and to combat diaper rash [67].

Mercury is also known to affect heart function by influencing hormones from the pituitary gland [89]. In test animals, mercury exposure increased the force of heart muscle contraction to cause high blood pressure by blocking the passage of calcium ions into heart muscle cells [90]. Mercury was also found to block the enzyme in the cell membrane that actively passes calcium in and out of the muscle cells by attaching to the thiol part of the enzyme [91].

It was reported that exposure to mercury by frequent consumption of fish had a strong positive correlation with increased arterial blood pressure [92]. Other studies also found some correlations between mercury exposure and increased risk of hypertension, myocardial infarction, coronary dysfunction, and atherosclerosis [93,94,95]. It was demonstrated that mercury exposure should be associated with the progression of atherosclerosis and an increased risk of developing cardiovascular disease [96]. Another mechanism by which mercury exerts toxic effects on the cardiovascular sys-

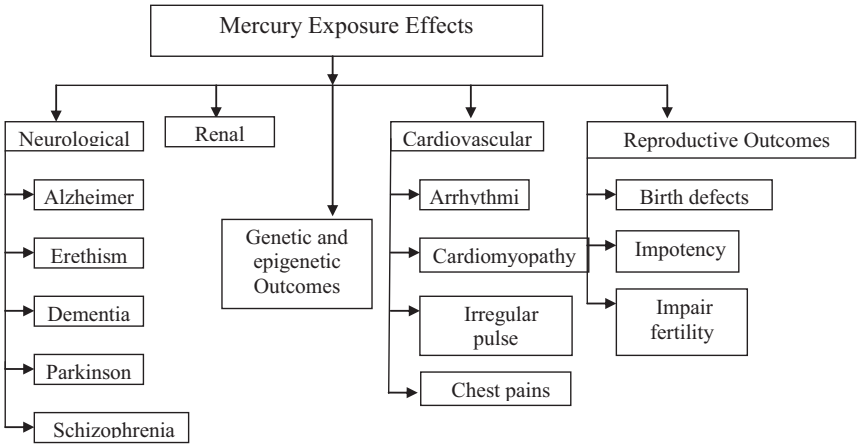


**Fig. 2.** Plot of human health effects induced by exposure to mercury.

tem is through the inactivation of the "paraoxonase" an enzyme that slows the low-density lipoprotein (LDL) oxidation process with an important antiatherosclerotic action [97]. Sherwani et al. [98]. investigated the mechanism of MeHg induced phospholipase D (PLD) activation through upstream regulation by phospholipase $A_2$ ($PLA_2$) and lipid oxygenases, e.g., cyclooxygenase (COX) and lipoxygenase (LOX) in bovine pulmonary artery endothelial cells. Their results showed that MeHg significantly contributed to the activation of both $PLA_2$ and PLD. The association between mercury exposure and increased risk of developing cardiovascular and neurological disease is thus apparent. The degree of severity of mercury exposure is hence comparable to traditional cardiovascular risk factors such as hypertension diabetes or hypercholesterolemia [88].

### 5.4. Reproductive outcomes

Many reports point to the fact that Hg can exert large effects on the reproductive functions of both males and females. The toxic effects of mercury exposure have been implicated in birth defects, attention deficit disorders, impotency, and significant reduction in sperm motility (and sperm count) leading to infertility [99]. Exposure to organic forms of mercury was found to cause low sperm count, a reduction in libido and impotence in some subjects [100]. Hatef et al. [101] also reported adverse effects of mercury on sperm motility.

An increased rate of spontaneous abortion in women was also observed when their spouses or partners were occupationally exposed to mercury vapor [102]. Chronic mercury exposure can seriously impair fertility, pregnancy, and newborn development [103]. Reproductive history and hair samples were taken from 45 female dentists and 31 dental nurses to assess their level of mercury exposure. Accordingly, a positive association was found between elevated methylmercury levels and incidences of malformation and aborted pregnancies [104]. Mercury exposure is also suspected as the potential cause of menstrual cycle disorders [103].

During pregnancy, mercury from the tissues of the mother passes readily through the placenta and into the extremely vulnerable developing fetus [67]. Mercury (inorganic) is also released through breast milk to the nursing infant [105]. In the last decade, the incidence of autism has increased tenfold, and attention deficient disorders increased greatly as well [106]. The cause of these rapid increases in infant reactive conditions is currently a topic of immense debate and litigation. One theory is that it results from earlier and higher usage of vaccines containing the mercury preservative thimerosol [106]. Another is exposure to mercury through the mother's blood (methylmercury) and milk (inorganic mercury) [107].

### 5.5. Genetic-epigenetic outcomes, diagnosis, and treatment

Several ecogenetic-based studies documented the genetic and epigenetic factors that may exert direct influences on the toxicokinetics or toxicodynamics of Hg [108]. Accordingly, Hg exposures are suspected to be related to epigenetic marks such as DNA methylation [109]. It was also suggested that exposure to Hg should be associated with DNA hypomethylation of brain tissue in the polar bear [110]. The effects of Hg were also investigated with respect to the DNA methylation status in mouse embryonic stem cells [111]. These authors found hypermethylation of *Rnd2* gene in Hg-treated mouse embryonic stem cells after 48 or 96 h of exposure.

In an animal study, Onishchenko et al. [112] also linked MeHg-associated epigenetic repression of brain-derived neurotrophic factor (BDNF) to depressive-like symptoms in young male mice. In a pilot study of 58 women, hypermethylation of the GSTM1 promoter in whole blood was found in those with blood Hg values above 2.9 mg $L^{-1}$ [113]. In a survey study covering a total of 131 dental professionals, Goodrich [114] reported that exposure to methylmercury (from fish consumption) and inorganic Hg (from dental amalgams) may be associated with altered DNA methylation at global repetitive elements (long interspersed elements, LINE-1) with candidate genes related to epigenetic processes (*DNMT1*) and protection against Hg toxicity (*SEPW1* and *SEPP1*).

The measurements of Hg levels in human body samples (hair, urine, blood, and organ) are useful for diagnostic estimation of exposures to mercury in various time or dosage scales (acute, chronic, or low dose). It is well known that excretory half lives of Hg are distinguished between different types of body samples. For instance, Hg levels in blood and urine samples, while being highly correlated to each other, are found to reflect the effect of recent exposure rather than that of total body burden. More specifically, the half life of Hg in the blood was estimated in the range of three to five days; however, there are many variables for such estimation, as one cannot fully account for the possibility of excretion or deposition (on solid organs) of Hg during such period [115]. In contrast, the half lives of Hg in certain organs like brain were found to be much longer than those of blood or urine [116]. Although biological exposure index (BEI) values were set for clinical (and/or investigation) purposes (e.g., 50 mcg/L in urine as the US federal BEI), the occasional findings of objective symptoms below such index value confirm the difficulty in establishing such guideline [115]. For the treatment of mercury poisoning, the use of chelation agents such as the dithiols sodium 2,3-dimercaptopropanesulfate (DMPS) and

meso-2,3-dimercaptosuccinic acid (DMSA) has been recommended along with some metal species (e.g., zinc and selenium) with the potential to induce metal binding proteins like metallothionein and selenoprotein-P [116]. However, their efficacy in the treatment of the various Hg pools needs to be investigated further to extend the area of the practical application.

## 6. Conclusion

The existence of multiple intake pathways of mercury, including air, food, water, pharmaceuticals, and cosmetics, accounts for its easy accessibility to humans. In particular, fish eating populations are at an increased risk of exposure. There are also numerous studies that demonstrate mercury toxicity as an occupational health hazard such as goldminers and dental personnel. Because low-dose mercury toxicity is relatively difficult to define, safety precautions are generally insufficient at the personal level.

Governments should first put great efforts to ensure mercury-free conditions for air, water, and food by making more stringent regulation systems against contaminating industrial units by ensuring proper disposal guides for mercury garbage and by encouraging Hg-free processes and procedures. Media and NGOs can also educate the masses about mercury hygiene. There should also be greater awareness among the general public about abstaining from mercury laced food, medicines, cosmetic products, and other livelihood products. Scientists should also collaborate actively to develop vaccines without using mercury as a preservative. All these efforts, if integrated into practice, will greatly help reduce the risk of Hg exposure.

In some fields, mercury must have already been phased out successfully like in the health care sector, mercury free measuring products, and disinfectants, as new technologies have been implemented in the chlorine alkali industry in a stepwise manner. Likewise, efforts have to be made to intensively mitigate the global mercury burden. In many developing countries, mercury is still a big problem which requires urgent action for proper control. The main focus of such efforts should be placed on removal of anthropogenic sources of mercury and prevention of exposure.

## Acknowledgements

This study was supported by a grant from the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science, and Technology (MEST) (No. 2009-0093848).

## References

[1] K.M. Rice, E.M. Walker Jr., M. Wu, C. Gillette, E.R. Blough, Environmental mercury and its toxic effects, J. Prev. Med. Public Health 47 (2) (2014) 74–83.
[2] H. Gibb, K.G. O'Leary, Mercury exposure and health impacts among individuals in the artisanal and small-scale gold mining community: a comprehensive review, Environ. Health Perspect. 122 (2014) 667–672, http://dx.doi.org/10.1289/ehp.1307864.
[3] J.D. Park, W. Zheng, Human exposure and health effects of inorganic and elemental mercury, J. Prev. Med. Public Health 45 (November) (2012) 344–352.
[4] J.M. Pacyna, E.G. Pacyna, Anthropogenic sources and global inventory of mercury emissions, in: M.B. Parsons, J.B. Percival (Eds.), Mercury: Sources, Measurements, Cycles, and Effects, Mineralogical Association of Canada, Ottawa, 2005.
[5] J. Nriagu, C. Becker, Volcanic emissions of mercury to the atmosphere: global and regional inventories, Sci. Tot. Environ. 304 (2003) 3–12.
[6] J. Olivier, J.S. Venter, C.Z. Jonker, Thermal and chemical characteristics of hot water springs in the northern part of the Limpopo Province, South Africa, Water SA 37 (2011) 427–436.
[7] T.W. Clarkson, L. Magos, The toxicology of mercury and its chemical compounds, Crit. Rev. Toxicol. 36 (8) (2006) 609–662.
[8] H.H. Kim, K.H. Kucharzyk, T. Zhang, M.A. Deshusses, Mechanisms regulating mercury bioavailability for methylating microorganisms in the aquatic environment: a critical review, Environ. Sci. Technol. 47 (6) (2013) 2441–2456.
[9] N. Basu, J.M. Goodrich, J. Head, Ecogenetics of mercury: from genetic polymorphisms and epigenetics to risk assessment and decision-making, Environ. Toxicol. Chem. 33 (6) (2014) 1248–1258.
[10] R.B. Turaga, Perceptions of mercury risk and its management, Hum. Ecol. Risk Assess. Int. J. 20 (2013) 1385–1405.
[11] F. Sprovieri, N. Pirrone, R. Ebinghaus, H. Kock, A. Dommergue, A review of worldwide atmospheric mercury measurements, Atmos. Chem. Phys. 10 (2010) 8245–8265.
[12] C.T. Driscoll, R.P. Mason, H.M. Chan, D.J. Jacob, N. Pirrone, Mercury as a global pollutant: sources, pathways, and effects, Environ. Sci. Technol. 47 (10) (2013) 4967–4983.
[13] United States Environmental Protection Agency (USEPA), Mercury: Human Exposure, (2011). http://www.epa.gov/hg/exposure.htm.
[14] N. Pirrone, S. Cinnirella, X. Feng, R.B. Finkelman, H.R. Friedli, J. Leaner, R. Mason, A.B. Mukherjee, G.B. Stracher, D.G. Streets, K. Telmer, Global mercury emissions to the atmosphere from anthropogenic and natural sources, Atmos. Chem. Phys. 1010 (2010) 5951–5964.
[15] D. Kocman, M. Horvat, Non-point source mercury emission from the Idrija Hg-mine region: GIS mercury emission model, J. Environ. Manag. 92 (2011) 2038–2046.
[16] D. Durnford, A. Dastoor, D. Figueras-Nieto, A. Ryjkov, Long range transport of mercury to the Arctic and across Canada, Atmos. Chem. Phys. 10 (2010) 6063–6086.
[17] S. Martínez-Trinidad, G.H. Silva, M.E.R. Islas, J.M. Reyes, G.S. Gregorio Solorio Munguía, Total mercury in terrestrial systems (air–soil–plant–water) at the mining region of San Joaquin, Queretaro, Mexico, Geofísica Internacional 52 (1) (2013) 43–58.
[18] D.W. Boening, Ecological effects, transport, and fate of mercury: a general review, Chemosphere 40 (2000) 1335–1351.
[19] X. Wang, C.W.N. Feng, Y. Anderson, Remediation of mercury contaminated sites—a review, J. Hazard Mater. 221–222 (2012) 1–18.
[20] S.J. Balogh, Y. Huang, H.J. Offerman, M.L. Meyer, D.K. Johnson, Episodes of elevated methylmercury concentrations in prairie streams, Environ. Sci. Technol. 36 (8) (2012) 1665–1670.
[21] J.L. Domagalski, C.N. Alpers, D.G. Slotton, T.H. Suchanek, S.M. Ayers, Mercury and methylmercury concentrations and loads in the Cache Creek watershed, California, Sci. Total Environ. 327 (1–3) (2004) 215–237.
[22] J. Zhu, T. Wang, R. Talbot, H. Mao, X. Yang, C. Fu, J. Sun, B. Zhuang, S. Li, Y. Han, M. Xie, Characteristics of atmospheric mercury deposition and size-fractionated particulate mercury in urban Nanjing, China, Atmos. Chem. Phys. 14 (2014) 2233–2244, http://dx.doi.org/10.5194/acp-14-2233-2014.
[23] P. Grandjean, Mercury, Institute of Public Health, University of Southern Denmark, Odense, Denmark; Department of Environmental Health, Harvard School of Public Health, Boston, MA, USA. (2008).
[24] A. Kowalski, M. Siepak, L. Boszke, Mercury Contamination of Surface and Ground Waters of Poznań, Poland, Pol. J. Environ. Stud. 16 (1) (2007) 67–74.
[25] D.E. MacCoy, Mercury concentrations in water, and mercury and selenium concentrations in fish from Brownlee Reservoir and selected sites in Boise and Snake Rivers, Idaho and Oregon, 2013, U.S. Geological Survey Open-File Report, 1099 (2014) 26. http://dx.doi.org/10.3133/ofr20141099.
[26] M. Horvat, V. Jereb, V. Fajon, M. Logar, J. Kotnik, J. Faganeli, M.E. Hines, J.C. Bonzongo, Mercury distribution in water, sediment and soil in the Idrijca and Soca river systems, Geochem. Explor. Environ. Anal. 2 (2002) 287–296.
[27] G. Qiu, X. Feng, S. Wang, L. Shang, Environmental contamination of mercury from Hg-mining areas in Wuchuan northeastern Guizhou, China, Environ. Pollut. 142 (2006) 549–558.
[28] J.J. Berzas-Nevado, L.F. García-Bermejo, R.C. Rodríguez Martín-Doimeadios, Distribution of mercury in the aquatic environment at Almaden, Spain, Environ. Pollut. 122 (2) (2003) 261–271.
[29] M. Patra, A. Sharma, Mercury toxicity in plants, Bot. Rev. 66 (3) (2000) 379–422.
[30] G.U. Chibuike1, S.C. Obiora, Heavy metal polluted soils: effect on plants and bioremediation methods, Appl. Environ. Soil Sci. (2014), http://dx.doi.org/10.1155/2014/752708, Article ID 752708.
[31] M.G. Kibra, Effects of mercury on some growth parameters of rice (*Oryza sativa* L.), Soil Environ. 27 (2008) 23–28.
[32] M.L. Søvik, Heavy metals in soil and water near mercury hotspots in Guizhou, China. (2008). Permanent link: http://urn.nb.no/URN:NBN:no-20859 BIBSYS: 092076300.
[33] L. Boszke, A. Kowalski, Total mercury in floodplain soils of the Warta River, Poland, Pol. J. Environ. Stud. 16 (4) (2007) 517–523.
[34] J.E. Gray, P.M. Theodorakos, D.L. Fey, D.P. Krabbenhoft, Mercury concentrations and distribution in soil, water, mine waste leachates, and air in and around mercury mines in the Big Bend region, Texas, USA, Environ. Geochem. Health (2014).
[35] A. Hayford, E.K. Amin, Impact of gold mining on soil and some staple foods collected from selected mining communities in and around Tarkwa Prestea Area, West Afr. J. Appl. Ecol. 14 (2008) 1–12.
[36] M.A. Hortellani, J.E.S. Sarkis, J. Bonetti, C. Bonetti, Evaluation of mercury contamination in sediments from Santos—São Vicente Estuarine System, São Paulo State, Brazil, J. Braz. Chem. Soc. 16 (2005) 1140–1149, 6.
[37] Environment Canada, Canadian Sediment Quality Guidelines for the Protection of Aquatic Life, Summary Tables (2004). http://www.ec.gc.ca.
[38] N.A. Hines, P.L. Brezonik, Mercury inputs and outputs at a small lake in northern Minnesota, Biogeochemistry 84 (2007) 265–284.

[39] A. Sam, D.K. Dodoo, D.K. Essumang, C.K. Adokoh, G.D. Nutifafa, Y. Ameyaw, Assessment of levels of cadmium and mercury of two estuaries in two regions of Ghana, Res. J. Appl. Sci. 5 (2010) 40–46.
[40] N. Pirrone, P. Costa, J.M. Pacyna, R. Ferrara, Mercury emissions to the atmosphere from natural and anthropogenic sources in the Mediterranean region, Atmos. Environ. 35 (2001) 2979–2986.
[41] A. Šípková, J. Száková1, P. Coufalík, O. Zvěřina, L. Kacálková, P. Tlustoš, Mercury distribution and mobility in contaminated soils from vicinity of waste incineration plant, Plant Soil Environ. 60 (2014) 87–92.
[42] M. Horvat, V. Jereb, V. Fajon, M. Logar, J. Kotnik, J. Faganeli, M.E. Hines, J.C. Bonzongo, Mercury distribution in water, sediment and soil in the Idrijca and Soca river systems, Geochem. Explor. Environ. A 2 (2002) 287–296.
[43] J. Jedrzejczak, Determination of total mercury in foods of plant origin in Poland by cold vapour atomic absorption spectrometry, Food Addit. Contam. 19 (10) (2002) 22–28.
[44] S.C. Dunagan, M.S. Gilmore, J.C. Varekamp, Effects of mercury on visible/near-infrared reflectance spectra of mustard spinach plants (*Brassica rapa* P.), Environ. Pollut. 148 (1) (2007) 301–311.
[45] B.V. Tangahu, S. Abdullah, H. Basri, M. Idris, N. Anuar, M. Mukhlisin, A review on heavy metals (As, Pb, and Hg) uptake by plants through phytoremediation, Hindawi Publishing Corporation, Int. Journal of Chem. Eng. (2011) 1–31, http://dx.doi.org/10.1155/2011/939161, 939161.
[46] United States Food and Drug Administration (USFDA), Mercury Levels in Commercial Fish and Shellfish (1990–2010), Retrieved July 1, (2011). http://www.fda.gov/Food/FoodborneIllnessContaminants/Metals/ucm115644.htm.
[47] M.M. Storelli, G.O. Marcotrigiano, Fish for human consumption: risk of contamination by mercury, Food Addit. Contam. 17 (2000) 1007–1011.
[48] J. Burger, M. Gochfeld, Mercury and selenium levels in 19 species of saltwater fish from New Jersey as a function of species, size, and season, Sci. Total Environ. 409 (2011) 1418–1429.
[49] R. Dabeka, A.D. McKenzie, D.S. Forsyth, H.B. Conacher, Survey of total mercury in some edible fish and shellfish species collected in Canada in 2002, Food Addit. Contam. 21 (5) (2004) 434–440.
[50] Z. Cheng, P. Liang, D.D. Shao, S.C. Wu, X.P. Nie, K.C. Chen, K.B. Li, M.H. Wong, Mercury Biomagnification in the Aquaculture Pond Ecosystem in the Pearl River Delta, Arch. Environ. Contam. Toxicol. (2011) 491–499.
[51] A.R. Olsen, B.D. Snyder, L.L. Stahl, J.L. Pitt, Survey design for lakes and reservoirs in the United States to assess contaminants in fish tissue, Environ. Monit. Assess. 150 (2009) 91–100.
[52] T.W. Clarkson, L. Magos, G.J. Myers, The toxicology of mercury—current exposures and clinical manifestations, N. Engl. J. Med. 349 (2003) 1731–1737.
[53] United Nations Environment Programme (UNEP), Mercury: A Priority for Action. Mercury Use in Healthcare Settings and Dentistry, (2010) 4. http://new.unep.org/hazardoussubstances/LinkClick.aspx?fileticket=yDKY6ZBMVbk%3d&tabid=4022&language=en-US.
[54] S. Decharat, P. Phethuayluk, S. Maneelok, P. Thepaksorn, Determination of mercury exposure among dental health workers in Nakhon Si Thammarat Province, Thailand, J. Toxicol. 2014 (2014), http://dx.doi.org/10.1155/2014/401012, Article ID 401012.
[55] M. Rathore, A. Singh, V.A. Pant, The dental amalgam toxicity fear: a myth or actuality, Toxicology International 19 (2012) 81–88.
[56] K.A. Ritchie, F.J.T. Burke, W.H. Gilmour, E.B. Macdonald, L.M. Dale, R.M. Hamilton, et al., Mercury vapour levels in dental practices and body mercury levels of dentists and controls, Br. Dent. J. 197 (10) (2004) 625–632.
[57] B. Karahalil, H. Rahravi, N. Ertas, Examination of urinary mercury levels in dentists in Turkey, Hum. Exp. Toxicol. 24 (8) (2005) 383–388.
[58] P.L. Drake, M. Rojas, C.M. Reh, C.A. Mueller, F.M. Jenkins, Occupational exposure to airborne mercury during gold mining operations near El Callao, Venezuela, Int. Arch. Occup. Environ. Health 74 (3) (2001) 206–212.
[59] M.A. Al-Batanony, G.M. Abdel-Rasul, M.A. Abu-Salem, M.M. Al-Dalatony, H.K. Allam, Occupational exposure to mercury among workers in a fluorescent lamp factory, Quisna Industrial Zone, Egypt, Int. J. Occup. Environ. Med. 4 (3) (2013) 149–156.
[60] S. Harakeh, N. Sabra, K. Kassak, B. Doughan, Factors influencing total mercury levels among Lebanese dentists, Sci. Total Environ. 297 (2002) 153–160.
[61] G.M. Abdel-Rasul, M.A. Abu-Salem, M.A. Al-Batanony, M.M. Al-Dalatony, H.K. Allam, Neurobehavioral, respiratory, and auditory disorders among mercury-exposed fluorescent lamp workers, Menoufia Med. J. 26 (2013) 58–62.
[62] R. Harari, F. Harari, L. Gerhardsson, T. Lundh, S. Skerfving, K. Broberg, Exposure and toxic effects of elemental mercury in gold-mining activities in Ecuador, Toxicol. Lett. 213 (2012) 75–82.
[63] J.C. Clifton, Mercury exposure and public health, Pediatr. Clin. North Am. 54 (2) (2007) 237 (e1-45).
[64] S. Nabi, Toxic Effects of Mercury, Springer India, 2014, http://dx.doi.org/10.1007/978-81-322-1922.
[65] D. Peplow, S. Augustine, Neurological abnormalities in a mercury exposed population among indigenous Wayana in Southeast Suriname, Environ. Sci. Processes Impacts 16 (2014) 2415–2422.
[66] L. Björkman, B.F. Lundekvam, T. Lægreid, Mercury in human brain, blood, muscle and toenails in relation to exposure: an autopsy study, Environ. Health 6 (2007).
[67] R.A. Bernhoft, Mercury toxicity and treatment: a review of the literature, J. Environ. Public Health (2012) 1–10, http://dx.doi.org/10.1155/2012/460508, 460508.
[68] M.M.E. Muidawi, M.A.M. Hagga, A.B. Mousa, M.M. Khir, Toxicity of mercury of mercury associated with dental amalgam filling, Int. J. Pharmacol. Toxicol. 4 (1) (2014) 5–10.
[69] A. Cesarani, C. Minoia, P.D. Pigatto, G. Guzzi, Mercury, dental amalgam, and hearing loss, Int. J. Audiol. 49 (1) (2010) 69–70.
[70] D. Echeverria, Neurobehavioral effects from exposure to dental amalgam: new distinctions between recent exposure and Hg body burden, FASEB J. 12 (11) (1998) 971–980.
[71] J.T.A. Ely, Mercury induced Alzheimer's disease: accelerating incidence? Bull. Environ. Contam. Toxicol. 67 (2001) 800–806.
[72] F.W. Sorensen, J.O. Larsen, R. Eide, J.D. Schionning, Neuron loss in cerebellar cortex of rats exposed to mercury vapor: a stereological study, Acta. Neuropathol. (Berl.) 100 (1) (2000) 95–100.
[73] J.S. Woods, N.J. Heyer, J.E. Russo, M.D. Martin, P.B. Pillai, F.M. Farin, Modification of neurobehavioral effects of mercury by genetic polymorphisms of metallothionein in children, Neurotoxicol. Teratol. 39 (2013) 36–44.
[74] M.R. Geier, D.A. Geier, Timerosal in childhood vaccines, neurodevelopmental disorders, and heart disease in the U. S, J. Am. Phys. Surg. 8 (1) (2003) 6–11.
[75] J. Mutter, Is dental amalgam safe for humans? The opinion of the scientific committee of the European Commission, J. Occup. Med. Toxicol. 6 (2011) 2–6.
[76] B. Sharma, S. Singh, N.J. Siddiqi, Biomedical implications of heavy metals induced imbalances in redox systems, Biomed Res. Int. (2014) 640754, http://dx.doi.org/10.1155/2014/640754.
[77] A.E.A. Moneim, The neuroprotective effect of berberine in mercury-induced neurotoxicity in rats, Metab. Brain Dis. 30 (2015) 935–942, http://dx.doi.org/10.1007/s11011-015-9652-6.
[78] X. Li, F. Qu, W. Xie, F. Wang, H. Liu, S. Song, T. Chen, Y. Zhang, S. Zhu, Y. Wang, C. Guo, T.S. Tang, Transcriptomic analyses of neurotoxic effects in mouse brain after intermittent neonatal administration of thimerosal, Toxicol. Sci. 139 (2) (2014) 452–465, http://dx.doi.org/10.1093/toxsci/kfu049, Epub 2014 Mar 27.
[79] M. Nylander, L. Friberg, D. Eggleston, L. Björkman, Mercury accumulation in tissues from dental staff and controls in relation to exposure, Swed. Dent. J. 13 (6) (1989) 235–243.
[80] P.O. Ozuah, Folk use of elemental mercury: a potential hazard for children? J. Nat. Med. Assoc. 93 (2001) 320–322.
[81] S. Díez, Human health effects of methylmercury exposure, Rev. Environ. Contam. Toxicol. 198 (2009) 111–132.
[82] R.K. Zalups, Molecular interactions with mercury in the kidney, Pharmacol. Rev. 52 (1) (2000) 113–143.
[83] B. Joan Tarloff, H. Lawrence Lash, Toxicology of the Kidney, Third ed., CRC Press, 2004, Aug 2.
[84] D.P. Basile, M.D. Anderson, T.A. Sutton, Pathophysiology of acute kidney injury, Compr. Physiol. 2 (2012) 1303–1353.
[85] J.O. Duruibe, M.O.C. Ogwuegbu, J.N. Egwurugwu, Heavy metal pollution and human biotoxic effects, Int. J. Phys. Sci. 2 (2007) 112–118.
[86] L.H. Lash, S.E. Hueni, D.A. Putt, R.K. Zalups, Role of organic anion and amino acid carriers in transport of inorganic mercury in rat renal basolateral membrane vesicles: influence of compensatory renal growth, Toxicol. Sci. 88 (2) (2005) 630–644.
[87] Y.M. Sin, W.F. Teh, W.F. Wong, Effect of long-term uptake of mercuric sulphide on thyroid hormones and glutathione in mice, Bull. Environ. Contam. Toxicol. 89 (2009) 847–854.
[88] B.F. Azevedo, L.B. Furieri, F.M. Peçanha, G.A. Wiggers, P.F. Vassallo, Toxic effects of mercury on the cardiovascular and central nervous systems, J. Biomed. Biotechnol. (2012) 949048, http://dx.doi.org/10.1155/2012/949048.
[89] T.W. Clarkson, J.B. Vyas, N. Ballatori, Mechanisms of mercury disposition in the body, Am. J. Ind. Med. 50 (10) (2007) 757–764.
[90] A.F. Castoldi, N. Onishchenko, C. Johansson, et al., Neurodevelopmental toxicity of methylmercury: laboratory animal data and their contribution to human risk assessment, Regul. Toxicol. Pharmacol. 51 (2) (2008) 215–229.
[91] M.C. Houston, The role of mercury and cadmium heavy metals in vascular disease, hypertension, coronary heart disease, and myocardial infarction, Altern. Ther. Health Med. 13 (2) (2007) S128–S133.
[92] J.K. Virtanen, S. Voutilainen, T.H. Rissanen, et al., Mercury, fish oils, and risk of acute coronary events and cardiovascular disease, coronary heart disease, and all-cause mortality in men in Eastern Finland, Arterioscler. Thromb. Vasc. Biol. 25 (1) (2005) 228–233.
[93] E. Guallar, M.I. Sanz-Gallardo, P. Van'T Veer, et al., Mercury, fish oils, and the risk of myocardial infarction, N. Engl. J. Med. 347 (22) (2002) 1747–1754.
[94] W.R. Bastos, J.P.O. Gomes, R.C. Oliveira, et al., Mercury in the environment and riverside population in the Madeira River Basin, Amazon, Brazil, Sci. Total Environ. 368 (1) (2006) 344–351.
[95] D. Fillion, F. Sousa Passos, M. Larribe, J.R.D. Guimarães, A preliminary study of mercury exposure and blood pressure in the Brazilian Amazon, Environ. Health (2006) 5.
[96] K. Yoshizawa, E.B. Rimm, J.S. Morris, et al., Mercury and the risk of coronary heart disease in men, N. Engl. J. Med. 347 (22) (2002) 1755–1760.
[97] J. Hulthe, B. Fagerberg, Circulating oxidized LDL is associated with subclinical atherosclerosis development and inflammatory cytokines (AIR study), Arterioscler. Thromb. Vasc. Biol. 22 (7) (2002) 1162–1167.

[98] S.I. Sherwani, S. Pabon, R.B. Patel, M.M. Sayyid, T. Hagele, S.R. Kotha, U.J. Magalang, K.R. Maddipati, N.L. Parinandi, Eicosanoid signaling and vascular dysfunction: methylmercury-induced phospholipase D activation in vascular endothelial cells, Cell. Biochem. Biophys. 67 (2) (2013) 317–329, http://dx.doi.org/10.1007/s12013-011-9304-3.
[99] L. Pribylova, S. Podzimek, Z. Ulcova-Gallova, J. Prochazkova, J. Bartova, Z. Rokyta, Bull spermatozoa under mercury stress, Reprod. Domest. Anim. 40 (5) (2005) 454–459, PMID.16149952.
[100] E. Mocevic, I.O. Specht, J.L. Marott, A. Giwercman, B.A. Jönsson, G. Toft, T. Lundh, J.P. Bonde, Environmental mercury exposure, semen quality and reproductive hormones in Greenlandic Inuit and European men: a cross-sectional study, Asian J. Androl. 15 (1) (2013) 97–104, http://dx.doi.org/10.1038/aja.2012.121.
[101] A. Hatef, S.M. Alavi, I.A. Butts, T. Policar, O. Linhart, Mechanism of action of mercury on sperm morphology, adenosine triphosphate content, and motility in *Perca fluviatilis* (Percidae; Teleostei), Environ. Toxicol. Chem. 30 (4) (2011) 905–914.
[102] A.H.B. Schuurs, Reproductive toxicity of occupational mercury: a review of the literature, J. Dent. 27 (4) (1999) 249–256.
[103] K. Neeti, T. Prakash, Effects of heavy metal poisoning during pregnancy, Int. Res. J. Environ. Sci. 2 (1) (2013) 88–92.
[104] I.F. Talamanca, Occupational risk factors and reproductive health of women, Occup. Med. (Lond.) 56 (8) (2006) 521–531.
[105] J.G. Dorea, Mercury and lead during breast-feeding, Br. J. Nutr. 92 (1) (2004) 21–40.
[106] B.J. Davis, H.C. Price, R.W. O'Connor, R. Fernando, A.S. Rowland, D.L. Morgan, Mercury vapor and female reproductive toxicity, Toxicol. Sci. 59 (2) (2001) 291–296.
[107] A. Doja, W. Roberts, Immunizations and autism: a review of the literature, Can. J. Neurol. Sci. 33 (4) (2006) 341–346.
[108] N. Basu, J.M. Goodrich, J. Head, Ecogenetics of mercury: from genetic polymorphisms and epigenetics to risk assessment and decision-making, Environ. Toxicol. Chem. 33 (6) (2014) 1248–1258.
[109] J.M. Goodrich, N. Basu, A. Franzblau, D.C. Dolinoy, Mercury biomarkers and DNA methylation among Michigan dental professionals, Environ. Mol. Mutagen. 54 (3) (2013) 195–203.
[110] J.R. Pilsner, A.L. Lazarus, D.H. Nam, Mercury-associated DNA hypomethylation in polar bear brains via the LUminometric Methylation Assay: a sensitive method to study epigenetics in wildlife, Mol Ecol 19 (2010) 307–314.
[111] Y. Arai, J. Ohgane, S. Yagi, Epigenetic assessment of environmental chemicals detected in maternal peripheral and cord blood samples, J. Reprod. Dev. 57 (2011) 507–517.
[112] N. Onishchenko, N. Karpova, F. Sabri, E. Castren, S. Ceccatelli, Long-lasting depression-like behavior and epigenetic changes of BDNF gene expression induced by perinatal exposure to methylmercury, J. Neurochem. 106 (2008) 1278–1287.
[113] C.W. Hanna, M.S. Bloom, W.P. Robinson, D. Kim, P.J. Parsons, F.S. vom Saal, J.A. Taylor, A.J. Steuerwald, V.Y. Fujimoto, DNA methylation changes in whole blood is associated with exposure to the environmental contaminants, mercury, lead, cadmium and bisphenol A, in women undergoing ovarian stimulation for IVF, Hum. Reprod. 27 (2012) 1401–1410.
[114] J. Goodrich, N. Basu, A. Franzblau, D. Dolinoy, Mercury biomarkers and DNA methylation among Michigan dental professionals, Environ. Mol. Mutagen. 54 (2013) 195–203.
[115] R.A. Bernhoft, Mercury toxicity and treatment: a review of the literature, J. Environ. Pub. Health 2012 (2012), Article ID 460508.
[116] J.P.K. Rooney, The role of thiols, dithiols, nutritional factors and interacting ligands in the toxicology of mercury, Toxicology 234 (2007) 145–156.
[117] X. Xu, A. Umme, C. Kyle, W. Xiaobin, Temporal variability of atmospheric total gaseous mercury in Windsor, ON, Canada, Atmosphere 5 (2014) 536–556, http://dx.doi.org/10.3390/atmos5030536.
[118] M.T. Parsons, D. McLennan, M. Lapalme, C. Mooney, C. Watt, R. Mintz, Total gaseous mercury concentration measurements at Fort McMurray, Alberta, Canada, Atmosphere 4 (2013) 472–493.
[119] X.W. Fu, X. Feng, Z.Q. Dong, R.S. Yin, J.X. Wang, Z.R. Yang, H. Zhang, Atmospheric gaseous elemental mercury (GEM) concentrations and mercury depositions at a high-altitude mountain peak in south China, Atmos. Chem. Phys. 10 (2010) 2425–2437.
[120] Q. Wan, X.B. Feng, L. Julia, W. Zheng, X.J. Song, S.J. Han, H. Xu, Atmospheric mercury in Changbai Mountain area, northeastern China—Part 1: the seasonal distribution pattern of total gaseous mercury and its potential sources, Envrion. Res. 109 (2009) 201–206.
[121] H.T. Nguyen, K.H. Kim, M.Y. Kim, S.M. Hong, Y.H. Youn, Z.H. Shon, J.S. Lee, Monitoring of atmospheric mercury at a Global Atmospheric Watch (GAW) site on An-Myun, Island, Korea, Water Air Soil Pollut. 185 (2007) 149–164.
[122] United States Food and Drug Administration (USFDA), Mercury Levels in Commercial Fish and Shellfish (1990–2010), (2011). Available at: http://www.fda.gov/Food/FoodborneIllnessContaminants/Metals/ucm115644.htm.
[123] Canadian Food Inspection Agency (CFIA), Total mercury results for sampling periods April 1, 2002–March 31, 2003 and April 1, 2003–October 7, 2004, (2002–2003 and 2003–2004).