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Mercury and its Associated Impacts on Environment and Human Health: A Review

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Abstract

Mercury exists naturally and as a man-made contaminant. The release of processed mercury can lead to a progressive increase in the amount of atmospheric mercury, which enters the atmospheric-soil-water distribution cycles where it can remain in circulation for years. Mercury poisoning is the result of exposure to mercury or its compounds resulting in various toxic effects depending on its chemical form and route of exposure. The major route of human exposure to methylmercury (MeHg) is largely through eating contaminated fish, seafood, and wildlife which have been exposed to mercury through ingestion of contaminated lower organisms. MeHg toxicity is associated with nervous system damage in adults and impaired neurological development in infants and children. Ingested mercury may undergo bioaccumulation leading to progressive increases in body burdens. Mercury has profound neurological, endocrine, reproductive, and fetotoxicity effects. Although most countries recognize the need to combat mercury pollution, controls are either nonexistence or inadequate. Based on articles reviewed, we recommend community education on need for a reduction in use of products that contain mercury. Dentists should reduce or eliminate the use of mercury amalgam and use pre-encapsulated amalgam instead of mixing their own if they are to continue using amalgam. Environment management agencies should expand existing national research on environmental and health effects of mercury.

Keywords: Mercury; Toxicity; Environment

Introduction

Mercury is one of the most toxic elements and a threat to wildlife because it accumulates and magnifies to unsafe levels in aquatic food chains (Munthe et al., 2007). It is rapidly transformed by microorganisms into organic compounds that tend to bioaccumulate and biomagnify in animals (Ronchetti et al., 2006). All mercury species are toxic, with organic mercury compounds generally being more toxic than inorganic species. Because of its high bioaccumulation, mercury concentrations escalate up the food chain and for example, predatory fish can have up to 106 times higher mercury concentrations than the ambient water (Joint FAO/WHO, 2006). The organic form of mercury is most toxic as it passes the blood-brain barrier owing to its lipid solubility. So the primary route of exposure to methylmercury (MeHg) for humans is consumption of fish (Habiba et al., 2017).

Since the beginning of the industry, anthropogenic activities like increased mining, high rate of fossil-fuel burning, wide spread use of raw materials containing mercury are some important contributors of mercury to the environment. The allowable mercury level set by World Health Organization (WHO) for drinking water is 1 μgL^{-1} (Azimi & Moghaddam, 2013). Mercury is also considered by the U.S. Environmental Protection Agency (EPA) as a highly dangerous element because of its accumulative and persistent character in the environment. The damage has vast implications with human beings at the top of food chain getting the worst of the deal owing to biomagnifications (Azimi & Moghaddam, 2013). The amount of Hg mobilized and released into the environment has increased since the beginning of the industrial age. Hg pollution is primarily due to human activities.

Mercury and its compounds are currently used in a number of countries, especially in industrial countries such as Iran. Mercury is applied in several different aspects including Batteries (Bernardes, Espinosa, & Tenório, 2003), measuring and control equipment: medical and other thermometers, blood

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pressure gauges, manometers, pressure valves, gyroscopes, Discharge lamps like fluorescent lamps, laboratory chemicals, electrodes and apparatus for analysis, color photograph paper, slimicides for paper production, explosives, fireworks, color photograph paper, pharmaceuticals: preservatives in vaccines and eye drops, disinfectants; skin lightening creams and soaps; herbal medicine, cosmetics: biocides in eye cosmetics, arm and leg bands, pesticides, especially for seed dressing.

Chemical Forms and Properties of Mercury

Mercury is classified as a heavy metal (atomic weight 200.59) and is well known as being among the most toxic of metals (World Health Organization, 2007). Mercury is a non-transition metal and is an extremely rare element in the earth's crust, having an average mass abundance of only 0.08 ppm (Sinicropi et al., 2010). Hg has three valence states (0, I and II), and exists in three main forms, each of which have different toxicities, implications for health and measures to prevent exposure (IPCS 2000). These three forms of mercury are elemental mercury or Quick silver (Hg^0, metallic mercury, and mercury vapor), inorganic mercury (Hg^+ and Hg^{2+}), and organic mercury such as methylmercury (CH_3Hg, MeHg) and ethylmercury (C_2H_5Hg, EtHg).

Elemental mercury

Elemental mercury (Hg) has a peculiar behavior, in that, it is monoatomic in the vapor phase, and has a relatively high vapor pressure at 20 °C (1.3 10^{-3} mm). It uniquely exists in liquid form at room temperature and quickly turns to vapor when heated above room temperature. The high volatility of Hg^0 prolongs the effects of anthropogenic releases through repeated atmospheric recycling to and from the land and the sea (Mason et ., 1994). Hg^0 can remain suspended in the atmosphere for up to 1 year, where it can be transported and deposited globally.

Elemental mercury is volatile at room temperature and the vapors may represent a hazard to humans. Such exposure may occur in laboratories, work places as well as in homes. In private homes, the broken thermometers containing mercury could become a source of exposure, as it can be very difficult to collect the spilled mercury. In many countries, the use of mercury in thermometers has now been banned as a policy to reduce the risk to consumer and the release of mercury into nature. Work place exposure may occur in many types of industries, where major uses of elemental mercury include chlorine-alkali manufacture, dental amalgams, electronic switches and fluorescent lamps.

Toxicokinetics: Elemental mercury exposure from the air is readily taken up through the lungs and about 74% is retained in the human body (Hursh et al., 1976). From blood, the elemental mercury distributes throughout the body, as it easily passes through most cell membranes including the blood-brain barrier and the placenta. In blood, the elemental mercury is oxidized to mercuric mercury partly under the influence of catalase (Carocci et al., 2014) and this influences brain uptake of mercury (Carocci et al., 2014). It has been shown that uptake of elemental mercury in the brain will decrease if the amount of catalase activity in the brain is inhibited (Eide & Syversen, 1982). The uptake of elemental mercury in brain tissue is also markedly dependent on brain glutathione levels, as a 20% reduction in brain GSH content will result in a 66% increase in brain mercury content (Eide & Syversen, 1982).

Toxic effects: Acute inhalation exposure, at high concentrations, may induce respiratory distress including dyspnea. Chronic exposure may induce symptoms from the central nervous system (CNS) including tremors, delusions, memory loss, and neurocognitive disorders. Many of the signs and symptoms associated with slight poisonings will eventually disappear after the exposure ends. However, severe exposure may result in a lasting effect on brain function. Additionally, long-term exposure may also cause effects in the kidney (Lohren et al., 2015).

Inorganic mercury compounds

Hg^0 is oxidized in air to its inorganic forms (Hg^+ and Hg^{2+}) and is released during rain events to be deposited in soil, or into the waters of rivers, lakes, and oceans. Inorganic mercury, derived from industrial release and from contaminated water, is biomethylated (in the aqueous environment and by phytoplankton in the ocean) to methylmercury (MeHg), primarily by sulfate-reducing bacteria (Morel et al. 1998). MeHg is accumulated to high concentrations in shellfish, predatory fish (i.e., swordfish, shark and king mackerel) and sea mammals. It is bioaccumulated especially by the liver, brain, kidney, and muscle (Compeau and Bartha 1985).

Inorganic mercury compounds have been used in a very extensive range of medical and cosmetic products; antiseptics, teething powders, skin-lightening creams. Accidental or intentional poisonings of mercuric chloride have not been uncommon. Inorganic mercury compounds can be either mercury in monovalent (mercurous – Hg^{2+}) or divalent (mercuric – Hg^{2+}) form. Mercurous chloride has very low solubility in water and is therefore regarded as non-hazardous. However, the use of teething powder containing mercurous mercury by infants led to a marked increase in their urinary mercury level (Warkany, 1966).

Toxicokinetics: Inorganic mercury accumulates primarily in the kidney, followed by its accumulation in the liver. The kinetics of mercuric mercury in humans (Lohren, Blagojevic, et al., 2015) demonstrate that about 1–16% of the initial dose is absorbed with a body half-time of about 41 days. No significant deposition of mercury was found in the head region for the first 58 days. Animal studies by Friberg et al. (1961) have shown that 8% of mercuric chloride applied to the skin can be absorbed in 5 h. In an experimental study on rats, it was shown that there is an uneven distribution of mercury in the nervous system. More mercury was found in the neurons compared to the glial cells, and the mercury had accumulated in lysosomes. The motor neurons contained more mercury than the sensory neurons and it was noted that mercury was present in the cerebellum, but not in the Purkinje cells.

Toxic effects: The organs primarily affected after acute poisoning of mercuric mercury are the intestine and kidneys. In the intestine, the corrosive effects will dominate while in the kidneys, renal failure may occur within 24 h due to necrosis of the tubular epithelium. As little as 1g can prove fatal to an adult human. The most prominent effect of mercuric mercury is tubular necrosis in the kidney and after prolonged exposure glomerulonephritis

can also be seen. Mercuric mercury may also cause autoimmune diseases (Stejskal, 2015).

Organic mercury

The rapid inter conversion of the inorganic forms into the organic ones, including the possibility of disproportionation reactions, means that the environmental behavior of Hg is complex (Rasmussen, 1994). Mercury has no known physiological role in humans and is among the most harmful heavy metals to which humans and wildlife can be exposed. Furthermore, the human body lacks effective mechanisms to excrete it. The organometallic compounds of mercury have a higher solubility in lipids than its inorganic species.

The organic mercury compounds include alkyl and phenyl groups as their organic molecular part. The phenylmercury compounds are mainly used as preservatives in medicine. Among the alkyl compounds, both the methyl and ethyl mercury compounds can be present in the environment. These compounds may exist as monoalkyl or dialkyl compounds (Carocci et al., 2014). The dialkyl compounds are very volatile and difficult to handle for any practical purpose including toxicology studies (Carocci et al., 2014). Further, these compounds are readily absorbed both through the airways and intact skin and are highly toxic even at very low exposure.

Human exposure to Mercury

Hg is released to the environment from both anthropogenic and natural sources. Natural sources include weathering of rocks and from geological movements. For instance annually, volcanic and geothermal activities release an estimated 1,500 tons of mercury to the environment (Maria et al., 2017; Sundseth et al., 2017). Anthropogenic release occurs from manifold industrial point sources and is estimated to constitute 2,320 tons of mercury emitted annually into the atmosphere (Nicola Pirrone et al., 2010).

Sources of Hg exposure resulting from human enterprise include industrial consumption of fossil fuels, cement production and incineration of solid wastes, contact with topical medicines, thermometers, barometers, and batteries, in addition to medical waste incineration, Hg-based substances used in ritualistic practices and dental amalgams (Maria et al., 2017; N. Pirrone et al., 2001). Autopsy studies have shown that dental amalgams are the main source of mercury in human tissues. Amalgam bearers have about 2–12 fold more mercury in their tissues, including the brain, than individuals without amalgams (Joachim Mutter, 2011).

In some countries, consumption of inorganic mercury preparations is a significant source of human intoxication. The reason for this is that such preparations have long been used as medications, germicidal soaps and skin creams (Guzzi and La Porta 2008). Some skin creams contain as much as 6–10 % mercurial chloride or calomel (Hg_2Cl_2). For many years, calomel was used in infant teething powders, worm drugs, and as an analgesic.

MeHg is an organomercurial compound primarily found as a pollutant in the aquatic environment. When MeHg is present in nature, its source is usually from biomethylation of inorganic mercury that is carried out by aquatic anaerobic sulfate-reducing bacteria (Morel et al., 1998). MeHg ultimately derives from anthropogenic sources, and when formed will be released into rivers, lakes, and oceans. Consequently, people, whose diet consists mainly of fish and shellfish, may be exposed to high levels of MeHg.

Absorption, Distribution, and Toxicity of Mercury

The toxicity of metals and metal compounds largely depends on the degree to which they are bioavailable, i.e. the degree to which they are absorbed through cell membranes, are distributed within the cell and bind to cellular macromolecules. When Hg^0 from dental amalgams is inhaled as a vapor into the lungs, about 80% is absorbed (Joachim Mutter et al., 2010).

Due to its uncharged monoatomic form, Hg^0 is highly diffusible and lipid soluble, and easily crosses the blood-brain barrier and lipid bilayers of cells and cell organelles, such as mitochondria. Mercury vapor also penetrates the mucosa and connective tissue of the oral and nasal cavities and may be transported into nerve cells (Joachim Mutter et al., 2010).

Exposure to toxic Hg^0 vapors may be either acute or chronic. Both acute and chronic Hg^0 exposures may result in human poisoning. In particular, such exposures can cause coughing, dyspnea, fever, tremors, malaise, axonal sensor motor polyneuropathy, gingivitis, hallucinations and mercurial erythrism, a syndrome that includes excitability, loss of memory, insomnia and neurocognitive disorders (Guzzi and La Porta 2008). Case-control studies have demonstrated an association between exposure to Hg^0 and the potential to develop amyotrophic lateral sclerosis (ALS).

In the inorganic form, mercury is absorbed from the gastrointestinal tract and acts to produce inflammatory reactions in the kidneys and gastrointestinal apparatus. Intracellularly, Hg^{++} is produced from metabolic oxidation of Hg^0. Research suggests that mercury induces autoimmune processes (Schiraldi & Monestier, 2009), and may be mutagenic at low concentrations (Schurz et al. 2000). Immunotoxic effects could potentially enhance susceptibility to infections, to malaria (Silbergeld et al., 1998) or immunologically-mediated diseases (McCabe & Lawrence, 1994).

Inorganic mercury accumulates in the human breast and is secreted in breast milk, which can damage the developing infant's central nervous system, pulmonary and nephrotic systems. Inorganic mercury exposure can also induce Kawasaki disease (Mutter & Yeter, 2008), which results from impairment of the immune system. The symptoms of children affected by Kawasaki disease include fever, photophobia, pharyngitis, oral lesions, skin rashes, and tachycardia, among others (Goyer & Clarkson, 1996).

Among the most dangerous mercury compound is dimethylmercury ($(CH_3)_2Hg$) which is toxic enough to cause death if only a few microliters is spilled on the skin, or even latex gloves (Joshi et al., 2012). Mercury poisoning can result in death, mental retardation, dysarthria, blindness, and neurological deficits, loss of hearing, developmental defects, and abnormal muscle tone (Guzzi & La Porta, 2008).

Impacts of Mercury on Environment and Human Health

Environmental impacts of mercury: The majority of mercury emissions to air are in the form of gaseous elemental mercury, which can be transported globally to regions far from the emis-

sions source. The remaining emissions are in the form of gaseous inorganic ionic mercury forms (such as mercuric chloride) or bound to emitted particles. These forms have a shorter atmospheric lifetime and will deposit to land or water bodies within roughly 100 to 1,000 kilometers of their source. The ocean currents are also media for long range mercury transport.

Air Pollution: Metallic, or elemental mercury, is a liquid at room temperature and like any other liquid, it evaporates into the air, where it can be inhaled. Very small amounts of metallic mercury, released into an enclosed space, can raise air concentrations of mercury to levels that may be harmful to health. The longer people breathe the contaminated air, the greater the risk to their health. In addition, metallic mercury and its vapors are extremely difficult to remove from clothes, furniture, carpet, and other porous items (Muhlendahl, 2015).

Some mercury sources in air are household products, including thermostats, glass thermometers, barometers, and switches in large appliances. Barometers have small openings in order to measure air pressure. Mercury vapors may be slowly released from them without breakage. Fluorescent bulbs contain a small amount of mercury vapor and a larger amount of mercury in a powder or dust form, whether accidental or intentional, spills of metallic mercury in a home or apartment (Muhlendahl, 2015).

Water Pollution: Water pollution refers to the additional to the water of an excess of material that is harmful to humans, animals and fishes (Aboud, 2010). The materials found in water and considered toxic to fish and other sea animals in one way or another can be recognized in oxygen debilitating materials, toxic gases, toxic organic compounds and pesticides, etc. The concentration of freshwater with a wide range of pollutants has become a matter of concern over the last few decades. The natural aquatic systems may be extensively contaminated with heavy metals released from domestic, industrial, mining and other man-made activities (Domagalski et al., 2004).

Health Impacts of Exposure to Mercury: Mercury is in widespread use in healthcare facilities. Thermometers and sphygmomanometers contain mercury and so do many medical batteries, fluorescent lamps, and electrical switches. Mercury compounds are also in preservatives, fixatives, and reagents used extensively in hospital laboratories. The impacts of mercury exposure are discussed in the subsequent sub-sections.

Nervous System: The nervous system is very sensitive to all forms of mercury. Methylmercury and metallic mercury vapors are more harmful than other forms because more mercury in these forms reaches the brain. Exposure to high levels of metallic, inorganic, or organic mercury can permanently damage the brain, kidneys, and developing fetus. Effects on brain functioning may result in irritability, shyness, tremors, changes in vision or hearing, and memory problems (Azimi & Moghaddam, 2013). Damage to the nerves of the arms and legs has been reported in employees with high exposures. Reduced sensation and strength in the arms and legs, muscle cramps and decreased nerve conduction have been observed.

Digestive and Renal Systems: Mercury is absorbed through the epithelial cells when ingested. This absorbed mercury can cause various digestive disturbances as it can inhibit the production of the digestive trypsin, chymotrypsin, and pepsin along with the function of xanthine oxidase and dipeptidyl peptidase IV (Vojdani et al ., 2003). The effects of mercury on the gastrointestinal system typically present as abdominal pain, indigestion, inflammatory bowel disease, ulcers and bloody diarrhea. Mercury ingestion has also been associated with the destruction of intestinal flora which can increase the amount of undigested food products in the bloodstream causing immune-mediated reactions and reduced resistance to pathogenic infection (Summers et al., 1993).

Various reports have shown mercury exposure can lead to various kidney injuries including subacute-onset nephrotic syndrome, tubular dysfunction, secondary focal segmental glomerulosclerosis, nephritic syndrome, nephrotic-range proteinuria, glomerular disease, and membranous glomerulonephritis (Oliveira et al., 1987).

Endocrine System: Low exposure levels of mercury may affect the endocrine system in animals and people by disruption of the pituitary, thyroid, adrenal glands and pancreas (Rice et al ., 2014). It is thought that mercury might impair endocrine function through its ability to reduce hormone-receptor binding (Iavicoli et al ., 2009). Hormones that appear to be the most affected by mercury are insulin, estrogen, testosterone, and adrenaline.

In addition, autopsy studies in 1975 revealed that the thyroid and pituitary retain more inorganic mercury than the kidneys. Mercury levels in the pituitary gland ranged from 6.3 to 77 ppb in one study, while another found the mean levels to be 28 ppb, levels found to be neurotoxic and cytotoxic (Nylander & Weiner, 1991). Low levels of pituitary function are associated with depression and suicidal thoughts and appear to be a major factor in suicide of teenagers and other vulnerable groups. Because of its effect on the pituitary, mercury is known to cause frequent urination as well as high blood pressure (McGregor & Mason, 1991).

Reproductive System: Mercury can precipitate pathophysiological changes along the hypothalamus-pituitary-adrenal and gonadal axis that may affect reproductive function by altering the circulating levels of follicle-stimulating hormone (FSH), luteinizing hormone (LH), inhibin, estrogen, progesterone, and the androgens (Davis et al., 2001). Reduced fertility among dental assistants with occupational exposure to mercury has been noted (Nagpal et al ., 2017). Studies in Hong Kong demonstrated that increased mercury levels were associated with infertility in both men and women (Dickman, Leung, & Leong, 1998). In males, mercury can have adverse effects on spermatogenesis (Martinez et al., 2017), epididymal sperm count, and testicular weight. Evidence also exists linking mercury with erectile dysfunction (Schrag & Dixon, 1985). In females, mercury has been shown to inhibit the release of FSH and LH from the anterior pituitary which in turn can affect estrogen and progesterone levels leading to ovarian dysfunction, painful or irregular menstruation, premature menopause, and tipped uterus (Chen et al., 2006). There is good evidence linking mercury with menstrual disorders including abnormal bleeding, short, long, irregular cycles, and painful

periods (Davis et al., 2001).

Fetotoxicity: In addition to reproductive issues, mercury is also associated with the fetotoxicity which can present as miscarriage, spontaneous abortions, stillbirth, and low birth weights (Aaseth, Hilt, & Bjørklund, 2018; Yoshida, 2002). In the neonate, mercury exposure during pregnancy has been linked to neural tube defects, craniofacial malformations, and delayed growth (Yoshida, 2002). Mercury is known to cross the placenta where it can inhibit fetal brain development resulting in cerebral palsy and psychomotor retardation in the latter stages of development (Castoldi et al., 2001).

In primates, maternal MeHg blood levels were moderately related to increased abortion rates and decreased pregnancy rates (Burbacher et al., 1984). MeHg easily enters through the placenta and damages the brain of the fetus. Babies may be born with a variety of birth defects (Finkelman & Tian, 2018). A study of 64 children exposed in utero to mercury and showed mercury associated damage including mental retardation (100%), primitive reflexes (100%), strabismus (77%), cerebellar ataxia (100%), dysarthria (100%), chorea and athetosis (95%), deformed limbs (100%), hypersalivation (95%), epileptic attacks (82%), and growth disorders (100%) (Harada et al., 1999).

Historical Cases Studies Depicting Health Impacts of Mercury

There are two epidemics that have occurred from MeHg poisoning events that are worthy of mention: The first case occurred in the Japanese villages of Minamata Bay (1953) and the second occurred in rural Iraq in 1971–1972 (Bakir et al., 1973).

Minamata disease is the term used to describe the poisoning that occurred among Japanese residents of Minamata Bay from ingesting methylmercury-containing fish and shellfish. Over a period of 36 years (1932–1968), the Chisso Corporation's chemical factory dumped about 27 tons of methylmercury-associated waste into Minamata Bay. MeHg is bioaccumulated within the food chain from plankton, microorganisms up to fish and shellfish. More than 10,000 Japanese living in the bay, who ate fish and shellfish contaminated with methylmercury, were afflicted by Minamata disease (Tsubaki & Irukayama, 1977). In the early 1950s, the people of Minamata Bay began to exhibit symptoms of neurological illness, i.e., uncontrollable trembling, loss of motor control, and partial paralysis. Newborn babies also exhibited symptoms of Minamata disease (Tsubaki & Irukayama, 1977).

The second epidemic of severe methylmercury intoxication resulted in the hospitalization of about 7,000 people and the death of 460 individuals in rural Iraq in 1971–1972 (Bakir et al., 1973). This incident occurred as a result of bread being prepared and eaten from wheat seed that had been treated with a mercury-based fungicide. The wheat seed was supposed to be planted, but labeling problems and other errors resulted in the treated wheat seed being used to bake bread. Both the Japanese and Iraq methylmercury poisoning incidents produced not only deaths, but multiple and long-lasting intoxication symptoms that included blindness, deafness, mental retardation, cerebral palsy, and dysarthria, especially in children exposed in utero (Guzzi & La Porta, 2008).

Conclusion

A number of body organ systems are affected by mercury in various forms. Evaluation of the consequences of mercury toxicity over the years has added greatly to the understanding of mercury toxicity and its human impact. History has left us with a wide array of information regarding the effects of mercury toxicity: the 1950s industrial spill in Minamata and Niigat Japan where it was defined as "Minamata disease", the rural poisoning in Iraq in 1971 to 1972 from MeHg-based fungicide and many among others not mentioned in this review. All of these events have left us with an indelible account of the detrimental effects of mercury on human health. In light of these historic events and the toxicological evidence presented in this review regarding the systemic effects of mercury include neurological, endocrine, reproductive, and embryonic development, and efforts should be made to insure adequate steps are taken to reduce the occurrence of mercury exposure and raise public awareness.

Recommendations

Based on the views from different scholars who have done research on mercury and its health and environment impacts, the following recommendations are important:

i. There is need for community education on need for a reduction in use of products that contain mercury. For instance, thermometers and thermostats are the two most obvious consumer products for which mercury-free alternatives exist.

ii. There is need to encourage dentists to reduce or eliminate the use of mercury amalgam and use pre-encapsulated amalgam instead of mixing their own if they are to continue using amalgam. Pre-encapsulated amalgam eliminates the need for elemental mercury in the dentist's office and the spills and dangers associated with elemental mercury.

iii. Whereas many studies have been conducted to assess health and environmental impacts of mercury, none has made an effort to establish mercury concentration in gray water (water from washing machines, showers, and sinks). There is need to ascertain mercury concentration in these waters to encourage actions that prevent the mercury-containing gray water from entering the sewer system.

iv. Combustion of fossil fuels, where Hg is emitted because of its presence in coal, oil, and gas, is an example of how mercury gets into the environment. This can be reduced using flue gas cleaning. All new generation sources using fossil fuels and waste incinerators should be equipped with efficient flue gas cleaning systems at the time of construction.

v. There is need for Environment management agencies, for instance, NEMA (for Uganda) to expand existing national research on environmental and health effects of mercury.

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