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Inorganic Mercury/Elemental Mercury

Toxicological Overview

Key Points

Kinetics and metabolism

- the main route of exposure to elemental mercury is inhalation and to inorganic mercury compounds is ingestion
- mercury is distributed to all tissues but mainly accumulates in the kidneys
- elemental mercury may readily cross the blood-brain barrier
- elimination predominantly occurs through the urine and faeces

Health effects of acute exposure

- inhalation of elemental mercury may cause respiratory, central nervous system and cardiovascular effects, renal damage and gastrointestinal disturbances
- ingestion of inorganic mercury compounds may affect the digestive tract, and cause renal damage, cardiovascular effects and skin/eye effects

Health effects of chronic exposure

- inhalation of elemental mercury vapour may cause neurotoxicity, nephrotoxicity and effects on the oral cavity
- ingestion of inorganic mercury compounds may cause neurotoxicity, digestive tract effects or renal failure
- the International Agency for Research on Cancer (IARC) classified elemental mercury and mercury compounds as a category 3 carcinogen, ie not classifiable as to the carcinogenicity to humans

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Summary of Health Effects

The main target organs of elemental and inorganic mercury toxicity are the central nervous system (CNS) and the kidneys. Inhalation is the significant route of exposure to elemental mercury. It is poorly absorbed from the gastrointestinal (GI) tract and is therefore unlikely to cause serious adverse health effects following ingestion. The majority of data available on the toxicity of inorganic mercury compounds concerns exposure by ingestion.

Acute inhalation of elemental mercury vapour may cause respiratory effects such as cough, dyspnoea, chest tightness, bronchitis and decreased pulmonary function. CNS effects include tremor, irritability, nervousness and hallucinations. Owing to the accumulation of mercury in the kidneys, acute renal failure, indicated by proteinuria, haematuria and oliguria, are commonly reported. Acute inhalation of elemental mercury may also cause GI effects such as stomatitis, abdominal pain, vomiting, diarrhoea and ulceration of the oral mucosa, as well as cardiovascular effects such as hypertension and tachycardia.

Inorganic mercury compounds are highly irritating to the GI tract and acute ingestion may cause a metallic taste, abdominal pain, vomiting, diarrhoea and necrosis of the intestinal mucosa, possibly leading to circulatory collapse and death. Ulceration of the mouth, lips, tongue and GI tract may also occur. If patients survive damage to the GI tract, acute renal failure may occur within 24 hours of ingestion. Hypertension and tachycardia have also been reported following ingestion of inorganic mercury compounds.

Acute dermal exposure to elemental mercury vapour can cause erythematous and pruritic skin rashes, and a reddening and peeling of the skin on the palms of the feet and hands associated with acrodynia. Contact with soluble inorganic mercury compounds may also cause irritation, vesiculation and contact dermatitis.

Chronic exposure to elemental mercury vapour by inhalation may cause neurotoxicity, the symptoms of which are decreased psychomotor skills and neuropsychological symptoms, including fatigue, tremor, headaches, depression, irritability and hallucinations. Nephrotoxicity including proteinuria and increased urinary enzyme excretion were observed following occupational exposure to elemental mercury, as well as stomatitis, sore gums and ulceration of the oral mucosa.

Following chronic ingestion of inorganic mercury compounds, irritability, weakness, insomnia, muscle twitching, swollen gums, excess salivation, anorexia and abdominal pain may occur.

There is little convincing evidence that exposure to mercury causes chromosomal damage or other mutagenic effects.

The International Agency for Research on Cancer (IARC) has classified elemental mercury and inorganic mercury compounds as category 3 carcinogens, ie not classifiable as to carcinogenicity to humans. There is limited data available on the carcinogenic effects of mercury in animals.

There is limited data available on exposure elemental or inorganic mercury during pregnancy. Conflicting results have been reported in studies investigating congenital malformations in the offspring of women occupationally exposed to mercury. The data does not indicate an increased risk of miscarriage or low birthweight following maternal occupational exposure. However, owing to a lack of data it is not possible to rule out an increased risk.

Kinetics and Metabolism

Elemental and inorganic mercury have different biological properties and hence are discussed separately.

Elemental mercury

The absorption of mercury is largely dependent on its form. The predominant route of exposure to elemental mercury is by inhalation of vapours. After inhalation, approximately 80% of mercury vapour crosses the alveolar membrane and is rapidly absorbed into the blood. Liquid elemental mercury is poorly absorbed (approximately 0.01%) from the GI tract, probably due to its conversion to divalent mercury and subsequent binding to sulfhydryl groups [1–3]. Dermal exposure to elemental mercury vapour may also occur to some extent, contributing to approximately 2.6% of the absorbed dose. Absorption by the olfactory nerves has also been proposed, although quantitatively this would be a minor pathway [3].

Absorbed elemental mercury is lipophilic, therefore it is distributed rapidly to all tissues. It accumulates to the greatest extent in the kidneys, accounting for 50–90% of the body burden [1, 3]. Its lipophilic nature also enables it to cross the blood-brain barrier and the barrier between the placenta and the fetus relatively easily [1]. Peak levels in all tissues are reached within 24 hours of exposure, apart from the brain where peak levels are only reached after 2–3 days [3].

Following inhalation, elemental mercury dissolves in the blood and some remains unchanged. It also undergoes oxidation in the red blood cells to form divalent mercury, which exists in a diffusible and non-diffusible form. The non-diffusible form exists as mercuric ion that binds to protein and is held in high molecular weight complexes that are in equilibrium with the diffusible form. In the plasma, divalent mercury mainly exists in the non-diffusible form and binds to albumin and globulins [3, 4]. Oxidation may also occur in the liver and lungs, although it may occur in most other tissues to a lesser extent. In the brain unoxidised mercury may be oxidised and thereby trapped, as the divalent form does not cross the blood-brain barrier as readily. Oxidation may also occur in the placenta and fetus [3].

Elemental mercury is predominantly eliminated through the urine and faeces, although some may be excreted in sweat, expired air or saliva, with the half-life being approximately 1–2 months [3, 5].

Inorganic mercury

For inorganic mercury, the predominant route of exposure is ingestion [3]. In humans, approximately 5–10% of inorganic mercury in food is absorbed after ingestion [3, 6]. The extent to which inorganic mercury is transported across the intestinal tract varies depending on the solubility and/or how easily the compound dissociates in the lumen to become available for absorption. Mercuric compounds (Hg^{2+}) are more readily absorbed than mercurous (Hg^{1+}) forms because of their solubility. In experimental animal studies, oral absorption of mercuric compounds has been shown to be dependent upon intestinal pH, diet and age [3].

No human studies have been found from which the absorption of inhaled inorganic mercuric compounds might be estimated. As with any inhaled aerosol, absorption will be determined principally by the size and solubility of the particles. In a study with dogs, using a mercuric oxide aerosol with a median particle diameter of 0.16 µm, the absorption was estimated to be approximately 45% [1]. The absorption of inorganic mercuric compounds by the lungs was described by an International Programme on Chemical Safety (IPCS) working group as “low”, this is probably due to the deposition of particles in the upper respiratory system and their subsequent clearance by the mucociliary escalator [3].

Inorganic mercury is distributed to all tissues following absorption, but due to the poor lipid solubility only a small fraction crosses the blood-brain barrier and the placenta. Following absorption, inorganic mercury is primarily distributed to the kidneys [4].

Elimination of inorganic mercury from the blood and brain is a biphasic process involving an initial rapid elimination phase followed by a slower phase. The main pathway of excretion of inorganic mercury is through the urine and faeces, with a half-life of approximately 1–2 months [1, 3]. Inorganic mercury is also excreted in breast milk [2, 3]. Reported mean concentrations of total mercury (from all exposures including food) in human milk in Europe range from 0.3–3.53 µg/L [7].

Sources and Route of Human Exposure

Mercury occurs naturally and is widely distributed in the environment owing to natural and anthropogenic processes. The major natural sources of mercury in the environment are degassing from the Earth's crust, emissions from volcanoes and evaporation from water bodies [1, 2]. Elemental mercury is also released into the environment following anthropogenic activities such as mining ore containing mercury, burning fossil fuels, industrial production of caustic soda and chlorine, production of cement and incinerating waste [2].

In the atmosphere, mercury mainly exists as elemental mercury vapour (90–99%), particle bound mercury (<5%) and gaseous divalent mercury (<5%) [2]. In the European Union (EU), reported levels of mercury in air range from 0.001–6 ng/m^3 in remote areas, 0.1–5 ng/m^3 in urban areas and 0.5–20 ng/m^3 in industrial areas [8].

Naturally occurring mercury in both ground and surface waters usually occurs at levels less than 0.5 µg/L. Mercury in drinking water is not considered a major source of exposure, except when significant pollution occurs [5].

Mercury enters soil indirectly by atmospheric deposition from both natural and anthropogenic sources [9]. A study by the British Geological Survey to define the normal background concentrations for soil contaminants in England found that mercury concentrations in urban areas were approximately 1.9 mg/kg and in all other areas were typically 0.5 mg/kg [10]. A similar study conducted in Wales found that level of mercury in soil, in non-urban areas, was approximately 0.25 mg/kg [9].

The general public may be exposed to mercury from accidental spillages following breakages of thermometers, barometers or electrical switches [1, 4]. Exposure to mercury may also occur from dental amalgam used in dental fillings. In the EU there is a move away from the use of mercury amalgam towards the use of alternative materials. The EU Scientific Committee on Emerging and Newly Identified Health Risks recently considered the safety of dental amalgam and concluded that "dental amalgam already in place is not considered a health risk for the general population" [11].

Exposure to mercury from the breakage of compact fluorescent lightbulbs (CFLs) can also occur. These lamps are now widely available on the market and are promoted as saving energy and reducing carbon dioxide emissions, particularly from coal fired power stations. The EU Scientific Committee on Health and Environmental Risks considers that short peak inhalation exposures to peak mercury concentrations in air occurring as a result of accidental breakage of CFLs are very unlikely to pose a health risk [12].

People may be exposed to inorganic mercury by ingestion because of the presence of mercury salts in some traditional herbal preparations [3, 7]. The use of illegal skin lighteners containing inorganic mercury compounds can result in significant exposure by dermal absorption [1, 13].

Occupational exposure to mercury may be a major source of exposure. Individuals working in the production of electrical equipment, thermometers or barometers, or those working in chemical processing plants or construction, could potentially be exposed to elemental mercury vapour or inorganic mercury [4]. Dentists and dental assistants involved with dental amalgam may also be exposed to elemental mercury by inhalation and, to a lesser extent, by skin contact [3, 4]. A workplace exposure limit (WEL) for mercury and divalent inorganic compounds has been set in the UK. The long term exposure limit (LTEL) is 0.02 mg/m^3 [8-hour time weighted exposure (TWA) reference period] [14].

Health Effects of Acute/Single Exposure

Human data

General toxicity

The major target organs of elemental mercury induced toxicity are the CNS and the kidneys. The cardiovascular and respiratory system, GI tract and the skin are also affected at higher concentrations. Similarly, the target organs following ingestion of inorganic mercury are the kidneys and the CNS [1].

Inhalation

Most data on the toxicity of mercury following inhalation refers to elemental mercury, as other forms, such as inorganic mercury, do not pose a significant risk by this route of exposure [4].

Elemental Mercury

Acute exposure to elemental mercury vapour can cause respiratory effects such as cough, dyspnoea and chest tightness. Bronchitis and bronchiolitis with interstitial pneumonitis, airway obstruction, and decreased pulmonary function have also been reported. In severe cases, pulmonary oedema, respiratory distress and fibrosis may occur. Patients commonly develop respiratory insufficiency [1, 3, 4, 15]. Such effects have been reported following exposure to 1.1–44 mg/m^3 of elemental mercury [15].

The CNS is one of the most sensitive targets following exposure to elemental mercury vapour [3]. The effects may include tremor, irritability, nervousness, memory loss, hallucinations and neuromuscular changes such as muscle atrophy and muscle weakness, headaches and decreases in cognitive function [1, 3].

The kidneys are a major target organ following exposure to elemental mercury vapour, due to the relatively high accumulation of mercury in the kidneys. High concentrations (not stated) have been reported to result in mild transient proteinuria, haematuria, oliguria, acute renal failure and degeneration of the proximal convoluted tubules [1, 3, 4].

GI effects have been reported in humans following acute inhalation of elemental mercury vapour. A classical symptom of mercury toxicity is inflammation of the oral mucosa, known as stomatitis, sometimes accompanied by excessive salivation and difficulty in swallowing. Other GI effects, including abdominal pain, nausea, diarrhoea, sore gums and ulceration of the oral mucosa, may also occur following inhalation of elemental mercury vapour, although few studies have reported the concentration of mercury at which such symptoms arise [1, 3, 4].

Hypertension and tachycardia have both been reported following inhalation of high concentrations of elemental mercury or inorganic mercury. Inhalation of elemental mercury may cause hepatocellular effects, hepatomegaly and central lobular vacuolation [3, 4].

Elemental mercury vapour has been reported to cause erythematous and pruritic skin rashes, reddening and peeling of the skin on the nose and palms of the feet and hands associated with acrodynia, burning eyes and conjunctivitis [3, 4].

Acute exposure to high levels of elemental mercury vapour may produce “metal fume fever” like symptoms, including fatigue, fever and elevated leukocyte count [4].

Ingestion

Most data on the toxicity of mercury following ingestion refers to inorganic mercury compounds. Elemental mercury is poorly absorbed from the GI tract and is therefore unlikely to cause serious adverse effects.

Inorganic Mercury

Ingestion of inorganic mercury salts such as mercuric chloride [mercury (II) chloride] is highly irritating to the GI tract. One of the earliest symptoms is a metallic taste, followed by gastric pain and vomiting. As the compound passes into the lower GI tract, abdominal pain, diarrhoea and necrosis of the intestinal mucosa may occur, possibly leading to circulatory collapse and death [15]. Ingestion of mercuric chloride may also lead to blistering and ulceration of the lips and tongue, oropharyngeal pain and ulceration of the GI tract [3, 4]. In contrast, ingestion of mercurous chloride [mercury (I) chloride] appears to cause less severe GI effects, although individual case studies have reported nausea, vomiting, swollen gums, excess salivation, diarrhoea, anorexia and abdominal pain following the ingestion of unknown concentrations of mercurous chloride [3, 4].

The kidney is a critical target organ following ingestion of inorganic mercury compounds. If patients survive GI tract damage following ingestion of mercuric chloride, oliguria, anuria, necrosis of the proximal tubule epithelium and acute renal failure may occur within 24 hours of exposure [1, 15].

Tachycardia and hypertension have been reported following ingestion of mercuric chloride and mercurous chloride [4].

Limited data is available regarding the respiratory effects following ingestion of inorganic mercury. Pulmonary oedema and shortness of breath have been reported following ingestion of mercuric chloride (dose not stated) [4].

Ingestion of inorganic mercury compounds may cause erythematous and pruritic skin rashes, reddening and peeling of the skin on the nose and palms of the feet and hands associated with acrodynia [3, 4].

Ingestion of mercuric chloride may cause jaundice and elevation of liver enzymes [3, 4].

Elemental Mercury

Ingestion of elemental mercury has little effect on the GI tract [4].

Dermal/ocular exposure

Elemental Mercury

Dermal exposure to elemental mercury vapour may cause erythematous and pruritic skin rashes, reddening and peeling of the skin on the palms of the feet and hands associated with acrodynia. Other signs and symptoms of acrodynia include severe leg cramps, irritability, fever, tachycardia, hypertension, excessive salivation or perspiration, fretfulness and weakness [4].

Dental amalgam fillings have occasionally been shown to cause local adverse effects in the mouth, such as allergic reactions [11]. In addition, dermatitis caused by allergy to elemental mercury has been described in dental personnel [1].

Inorganic Mercury

Soluble inorganic mercury compounds, in particular mercuric chloride, are irritating to the skin and mucous membranes. Exposure to 1-5 % may cause irritation, vesiculation, contact dermatitis and corrosion of the skin [3, 15]. Insoluble compounds are not immediately irritating but irritation may slowly develop as the compound is absorbed and ionised in tissues [15].

Animal and in-vitro data

Inhalation

Elemental Mercury

Mice, guinea pigs and rats inhaling elemental mercury vapour died of pulmonary oedema following exposure for 24–48 hours to an unknown concentration of vapour following a spillage of mercury droplets [4].

Cellular degeneration with necrosis of the heart tissue was observed in rabbits following exposure to 28.8 mg/m^3 of elemental mercury vapour for 4–30 hours. In the same study, GI effects were noted, ranging from mild pathological changes to significant cellular degeneration and necrosis of the colon, as well as hepatic effects, ranging from moderate pathological changes (unstated) to severe liver necrosis [4]. Rabbits also showed signs of renal effects, ranging from cellular degeneration to tissue destruction and necrosis following inhalation of 28.8 mg/m^3 of elemental mercury vapour for 2–30 hours [4].

Ingestion

Elemental Mercury

Ingestion of elemental mercury results in negligible absorption and therefore exerts little toxicological effect [4].

Inorganic Mercury

Limited data is available regarding the toxicity of inorganic mercury following oral exposure.

Rats administered a single gavage dose of mercuric chloride (7.4 or 9.2 mg/kg) showed no differences in body weight or liver weight compared to controls, although lactate dehydrogenase (LDH) activity was significantly decreased at both doses [4].

Renal toxicity was observed in rats and mice following acute exposure to mercuric chloride. Male and female rats were exposed to mercuric chloride (0.93–14.8 mg/kg a day) by gavage for 5 days a week. There was a significant increase in the kidney weights in groups exposed to 1.9 mg/kg a day and higher. Tubular necrosis occurred in rats exposed to 3.7 mg/kg a day and higher, the severity increasing in a dose-dependent manner. An increase in urinary levels of alkaline phosphatase, aspartate transaminase (AST) and LDH was also observed in such groups [4].

Minor renal tubular damage and rapid regeneration of the tubular epithelium were observed in mice given a single dose of 10 mg/kg of mercuric chloride by gavage [4].

Health Effects of Chronic/Repeated Exposure

Human data

General toxicity

Chronic exposure to mercury may affect the CNS, GI tract, kidneys, oral cavity, lungs, eyes, reproductive system and skin.

Inhalation

Elemental Mercury

Effects on the CNS are generally considered to be the most sensitive indicator of toxicity of elemental mercury vapour [1, 3]. A number of personality, cognitive, sensory and motor disturbances are associated with long term inhalation of elemental mercury vapour. Effects reported include tremors, insomnia, memory loss, neuromuscular changes, headache, polyneuropathy, unsteady walking, poor concentration, tremulous speech and blurred vision The symptoms may intensify and in some cases become irreversible with increasing exposure duration and/or concentration [3].

Several occupational studies have concluded that mild sub-clinical signs of CNS toxicity can be observed in workers exposed to elemental mercury at a concentration of 20 µg/m^3 or more for several years [3].

Occupational exposure to elemental mercury vapour may also result in kidney damage, indicated by proteinuria, increased urinary excretion of β-galactosidase, transferrin, β2-microglobulin or albumin, and proximal tubular and glomerular changes [1, 4]. An increased incidence of proteinuria has been reported in several occupational studies where workers were exposed to mercury vapours at concentrations of 2–30 µg/m^3 for long periods of time [2].

Effects of chronic inhalation of elemental mercury on the cardiovascular system are equivocal as studies have reported differing results. Two studies reported that after exposure to mercury (0–0.27 mg/m^3 in one study and an average of 0.075 mg/m^3 in the other) for more than 6 or 7 years, no effects were observed on blood pressure or electrocardiography. In contrast, workers exposed to 0.03 mg/m^3 for at least 5 years showed signs of palpitations and cardiovascular reflex responses were slightly reduced. Exposure to elemental mercury vapour has also been reported to cause hypertension and tachycardia, although the concentrations were not stated [4].

Some occupational studies indicate that there may be effects on the thyroid at exposure levels similar to those producing minor effects on the CNS and kidneys [2].

Ingestion

Inorganic Mercury

Limited data is available regarding the toxicity of inorganic mercury following chronic exposure through ingestion. Dementia, irritability and renal failure have been reported in 2 women following chronic ingestion (2 tablets a day for 6 and 25 years, respectively) of laxative tablets that contained 120 mg of mercurous chloride. The patients both died from inorganic mercury poisoning [4].

In the past, children treated with products containing mercurous chloride (such as teething powders) exhibited signs of irritability, weakness, insomnia, photophobia, muscle twitching or confusion [3]. GI effects such as swollen gums, excess salivation, anorexia, diarrhoea or abdominal pain were also seen in children treated with mercurous chloride [3, 4].

Genotoxicity

Data from 14 studies of cytogenetic effects, such as sister chromatid exchange, micronucleus formation, chromosomal aberrations, aneuploidy and polyploidy in peripheral blood lymphocytes of individuals exposed to elemental mercury or mercury compounds, were inconclusive. Overall, such monitoring studies have provided little convincing evidence that exposure to mercury causes chromosomal damage [2, 3].

Carcinogenicity

There is inadequate evidence in humans for the carcinogenicity of mercury and mercury compounds. IARC in 1993 classified elemental mercury and inorganic mercury compounds as category 3 carcinogens, ie not classifiable as to carcinogenicity to humans [16].

Reproductive and developmental toxicity

Several studies have shown that chronic inhalation of elemental mercury has no effect on female fertility. Menstrual cycle disorders were reported to be more frequent in women occupationally exposed to elemental mercury [1, 3].

There is limited published data available relating to exposure to inorganic or elemental mercury during pregnancy. Studies investigating congenital malformations in the offspring of women occupationally exposed to inorganic or elemental mercury have reported conflicting results. The available data does not indicate an increased risk of miscarriage or low birthweight following maternal occupational exposure to mercury; however, the UK National Teratology Service (UKTIS) concluded that the “data are too limited to exclude an increased risk”. Where exposure to mercury occurs during pregnancy, maternal toxicity is likely to be a determinant of risk to the fetus [17].

In 1997, the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment concluded that there was no evidence that occupational exposure to mercury during pregnancy in modern dental practices was harmful [18].

Males exposed to elemental mercury vapour in an occupational setting showed no association between mercury exposure and decreased fertility, or with increased rates of major malformations or serious childhood disease in their offspring [1].

Animal and in-vitro data

Inhalation

Elemental Mercury

Respiratory effects have been observed following chronic exposure to elemental mercury vapour. Rats exposed to 1 mg/m^3 of mercury vapour for 100 hours a week for 6 weeks showed signs of lung congestion, whereas rats exposed to 3 mg/m^3 for 3 hours a day, 5 days a week for 12–42 weeks, showed no significant changes [4].

Mild to moderate pathological changes in the hearts of rabbits were observed following exposure to 0.86–6 mg/m^3 of elemental mercury vapour for 2–12 weeks [4].

No GI changes were observed in rabbits exposed to 6 mg/m^3 for 7 hours a day, 5 days a week, for up to 11 weeks, although hepatic changes were reported, ranging from moderate pathological changes to marked cellular degeneration and necrosis [4].

In rats, slight degenerative changes were seen in the renal tubular epithelium following inhalation of 3 mg/m^3 of mercury vapour for 3 hours a day, 5 days a week for 12–42 weeks [4].

Ingestion

Inorganic Mercury

Studies in animals have indicated that nephrotoxicity is the most sensitive endpoint following repeated exposure to inorganic mercury compounds [2]. Sub-acute studies (6 months) in rats given mercuric chloride orally, indicated a NOAEL of 0.23 mg/kg a day. Evidence of nephrotoxicity was seen at 0.46 mg/kg bw/day and higher dose levels. Studies have also been reported on the Brown Norway rat, a species prone to the development of mercuric chloride induced glomerulonephritis. Some evidence of effects were seen following oral doses of 3 mg of mercuric chloride once a week for 60 days; this was considered to be the LOAEL (the daily dose was estimated to be around 0.3 mg/kg bw/day) [2].

Respiratory effects such as forceful and laboured breathing, nose bleeds and other unspecified breathing difficulties were observed in rats following dietary exposure to 2.2 mg/kg a day of mercuric chloride for 3 months [4].

Several studies reported cardiovascular effects following oral exposure to inorganic mercury. Exposure of rats to 28 mg/kg bw/day of mercuric chloride in drinking water for 180 days resulted in hypertension and a decrease in cardiac contractility, but did not affect heart rate. In contrast, exposure of a different strain of rat to 7 mg/kg bw/day mercuric chloride in

drinking water for 360 days resulted in hypertension and increased cardiac contractility as well as decreased baroreceptor reflex sensitivity [4].

Genotoxicity

No experimental data was available on the genotoxicity of elemental mercury.

Studies with mercuric chloride have given conflicting results [16]. Single strand DNA breaks have been reported following exposure of cultured mice embryo cells and Chinese hamster ovary cells to mercuric chloride. Other studies reported the induction of gene mutations in mouse lymphoma cells and DNA damage in rat and mouse fibroblasts. In contrast, mercuric chloride did not induce chromosomal aberrations in human lymphocytes in vitro [1]. No in-vivo data is available. However, the data from the carcinogenicity studies does not suggest that inorganic mercury compounds have significant mutagenic potential.

Carcinogenicity

There is inadequate evidence in experimental animals for the carcinogenicity of metallic mercury and limited evidence for the carcinogenicity of mercuric chloride [16]. Following oral exposure to mercuric chloride (equivalent to 1.9 and 3.7 mg/kg bw/day expressed as mercury) for 2 years, male rats in the 3.7 mg/kg bw/day group showed an increased incidence of squamous cell papillomas of the forestomach and thyroid follicular cell carcinomas compared with controls [2, 4]. The forestomach tumours were thought to have developed as a result of direct irritation of the tissue so would be unlikely to have any relevance at lower doses [2]. In similar studies in mice administered mercuric chloride by gavage for 2 years (3.7 or 7.4 mg/kg bw/day expressed as mercury) renal tubule tumours were evident in 3 of the 49 males exposed to the higher dose [2, 4]. The kidney tumours occurred at doses that were also nephrotoxic and would be expected to arise by a non-genotoxic mechanism [2].

Reproductive and developmental toxicity

Limited data is available regarding the reproductive toxicity of inorganic mercury. Male mice injected with single doses of mercuric chloride (1 mg/kg) showed decreased fertility, with normal fertility resuming after approximately 2 months [1]. Male rats treated with intraperitoneal doses of 0.05–0.1 mg/kg of mercuric chloride over 90 days showed a gradual alteration in testicular tissue, such as a decrease in seminiferous tubular diameter, spermatogenic cell counts and Leydig cell nuclear diameter [1].

Female mice administered 0.25, 0.5 or 1 mg/kg bw/day of mercuric chloride by gavage from 21 days prior to ovulation and throughout mating, gestation and lactation period showed no significant increase in the rate of malformation compared with control animals. However, decreased fertility was observed at all doses, and a decreased rate of offspring survival after exposure to the highest dose [17].

Pregnant mice administered single daily doses of mercuric oxide (25–125 µg/g) by gavage from day 4 to day 12 of gestation showed a dose-dependent increase in late resorption and decreased fetal weight. Teratogenic effects occurred more frequently in the exposed litters, although no dose-dependent effect was observed [17].

In a low dose, 2 generation study, Wistar rats exposed to mercuric chloride (at an average equivalent to 0.022–0.029 mg/kg bw/day of mercury) in drinking water, showed reduced bodyweight and reduced lifespan in all generations. The number of litters from the treated parental generation was higher than that in controls, comparable to controls in the F_1 and statistically lower than controls in the F_2 generation. The number of pups per litter was also significantly reduced in the F_2 generation exposed to mercuric chloride compared with controls. Although this study reported these effects at low levels, it is noted that only 1 dose was used and 10 animals were used in each group. Additionally, the study reported a 90–100% survival to 3 years of age in untreated control groups. Such a high survival rate in control Wistar rats would not be expected at 3 years of age. It is noted, however, that adverse effects on fertility/litter size, postnatal survival and offspring body weight in rats were also reported by another research group in 2 earlier multi-generation studies, although NOAELs were not established in these studies [7].

Ototoxicity was reported in mice following exposure to mercuric chloride prenatally, perinatally and/or post weaning at a dose equivalent to 0.37 mg/kg a day expressed as mercury [7].

References

1. International Programme on Chemical Safety (IPCS). Inorganic Mercury. Environmental Health Criteria 118, 1991. World Health Organization: Geneva.
2. Environment Agency (EA). Contaminants in soil: updated collation of toxicological data and intake values for humans: mercury. In Science Report SC0500212009. EA: Bristol.
3. International Programme on Chemical Safety (IPCS). Elemental Mercury and Inorganic Mercury Compounds: Human Health Aspects. Concise International Chemical Assessment Document No. 50, 2003. World Health Organization: Geneva.
4. Agency for Toxic Substances and Disease Registry (ATSDR). Toxicological Profile for Mercury, 1999. US Department of Health and Human Services: Atlanta, US.
5. World Health Organization (WHO). Mercury in Drinking Water. Background document for development of WHO Guidelines for Drinking-water Quality, 2005. World Health Organization: Geneva.
6. Environment Agency (EA). Soil guideline values for mercury in soil. In Science Report SC0500212009. EA: Bristol.
7. European Food Safety Authority (EFSA). Scientific opinion on the risk for public health related to the presence of mercury and methylmercury in food. EFSA J, 2012;10(12):2985.
8. World Health Organization (WHO). Air Guidelines for Europe. WHO Regional Publications, European Series, No. 91, 2nd Edition, 2000. WHO Regional Office for Europe: Copenhagen.
9. Department for Environment, Food and Rural Affairs (Defra). Technical guidance on normal levels of contaminants in Welsh soil: Hg. R&D Project SP1008, January 2013. British Geological Survey: Keyworth; and Defra: London.
10. British Geological Survey (BGS). Technical guidance sheet (TGS) on normal levels of contaminants in English soils: mercury, 2012. British Geological Survey: Keyworth.
11. Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR). The Safety of Dental Amalgam and Alternative Dental Restoration Materials for Patients and Users, 2015. European Union: Brussels.
12. Scientific Committee on Health and Environmental Risks (SCHER). Opinion on Mercury in Certain Energy-saving Light Bulbs – Exposure of Children, 2012. European Union: Brussels.
13. World Health Organization (WHO). Preventing Disease Through Healthy Environments – Mercury in Skin Lightening Products, 2011. World Health Organization: Geneva.
14. Health and Safety Executive (HSE). EH40/2005 Workplace Exposure Limits, 2nd Edition, 2011. The Stationery Office: London.
15. International Programme on Chemical Safety (IPCS). INCHEM, Mercury. Monograph for UKPID, 1996 London. http://www.inchem.org/pages/ukpids.html.
16. International Agency for Research on Cancer (IARC). Beryllium, cadmium, mercury and exposures in the glass manufacturing industry. IARC monographs on the evaluation of carcinogenic risk to humans, Volume 58, 1997. International Agency for Research on Cancer: Lyon.
17. UK Teratology Information Service (UKTIS). Exposure to inorganic and elemental mercury in pregnancy, 2012.
18. Committee on Toxicity of Chemicals in Food Consumer Products and the Environment (COT). Statement on dental amalgam, 1997. Department of Health: London.

This document from the PHE Centre for Radiation, Chemical and Environmental Hazards reflects understanding and evaluation of the current scientific evidence as presented and referenced here.

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