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MINIREVIEW

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Mercury exposure and its effects on fertility and pregnancy outcome

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Abstract

Mercury (Hg), a highly toxic environmental pollutant, shows harmfulness which still represents a big concern for human health, including hazards to fertility and pregnancy outcome. Research has shown that Hg could induce impairments in the reproductive function, cellular deformation of the Leydig cells and the seminiferous tubules, and testicular degeneration as well as abnormal menstrual cycles. Some studies investigated spontaneous abortion and complicated fertility outcome due to occupational Hg exposure. Moreover, there is a relation between inhaled Hg vapour and reproductive outcome. This MiniReview evaluates the hypothesis that exposure to Hg may increase the risk of reduced fertility, spontaneous abortion and congenital deficits or abnormalities.

KEYWORDS

dental amalgam, dental personnel, fertility, foetus, mercury

1 | INTRODUCTION

The problem of environmental pollution from mercury (Hg) and its effect on human health is currently a global issue.[1,2] Contamination of the biosphere by Hg is mainly caused by anthropogenic factors, including coal combustion, mining, cement production and chemical industry.[3-5] When Hg is released into the natural environment, and in groundwater, microorganisms including bacteria are often responsible for the biotransformation of the metal leading to the formation of methylmercury (MeHg).[6,7] Methylmercury and ethylmercury (EtHg) are highly hazardous forms that accumulate in freshwaters, ecosystems and food chains, leading to Hg exposure in people and other natural living organisms.[8-10] Worldwide, global recognition of the great concern caused by Hg pollution led to the adoption of the Minamata Convention on Mercury in 2017.[11] In July 2017, the 13th International Conference on Mercury as a Global Pollutant, which was held in the United States, was devoted to integrating Hg science and politics in the modern world.[12] Key issues for researchers and healthcare professionals were (a) environmental risk assessment; (b) biomonitoring, focusing on the effects of Hg on the health of children; (c) effects on the dental workers and general population; (d) interactions with nutrients; (e) the risk of EtHg in medical therapeutics; (f) genetic effects of Hg; and (g) effectiveness of measures to reduce the adverse effects of exposure with Hg.[12-15] It follows that additional efforts are needed to integrate the results of scientific research with political strategies to obtain the development of appropriate management tools. For example, the impact of Hg on human reproductive health is of particular concern.[16-18] It has been demonstrated that chronic exposure to inorganic Hg in laboratory hamsters, mice and rats may disturb the oestrous cycle,[19] impair embryo implantation and hamper follicular development.[20] Mercury accumulates in the pituitary and thyroid glands and the brain.[21-23] In rats, ovaries that are exposed to mercury oxides (HgO) showed alterations in the tissue histology and morphology, with a strong reduction in the number of follicles (either primordial, primary or Graaf follicles).[24]

In the fruit fly, *Drosophila melanogaster,* MeHg causes disorders in sexual mating. In male and female flies treated with MeHg concentrations ranging from 28.25 to 56.5 µmoles/L, copulation normally occurs, whereas flies treated with higher MeHg concentrations, that is, from 113 to 339 µmoles/L, failed in sexual copulation and cannot go ahead in the reproduction.[25] While the different government regulatory panels for the maximal Hg threshold in the environment and groundwaters established the range 0.050-2 µg/L, that is, 0.00025-0.01 µmoles/L, pollution might reach much higher values upwards in the food chain; for example, in yellowfin tuna (*Thunnus albacares*), MeHg load ranged from 0.03 to 0.82 µg/g wet weight across any individual fish, that is, 0.36-9.84 mg Hg (0.6-16.4 µmoles/L) for the whole animal.[26] Eating a simple can of Hg-polluted tuna, therefore, may represent intakes from 0.01 to 0.287 µmoles Hg, which accumulates in the body.[27-31]

The role of Hg as a toxicant in sexual reproduction and pregnancy is quite neglected compared with the great attention spent on reports regarding neurotoxicology from this heavy metal. Despite some contradictory evidence, the role of Hg in human reproduction is going to be a major alarming issue.[32-37] This MiniReview is aimed at analysing the published documentation about the effects of organic and inorganic Hg in human fertility, the outcome of childbirth, congenital abnormalities, loss of pregnancy and menstrual disorders.

2 | INSIGHTS ON THE ENVIRONMENTAL INDICES OF EXPOSURE OF MERCURY

2.1 | Mercury contents in the air

In order to give insightful evidence about Hg toxicology in human beings, firstly, we would like to address its pollution dynamics. An indicator of air pollution control in most countries is used when defining the emission limit of the pollutant. Coal mining and cinnabar mining are the main sources of Hg air pollution, particularly in China.[38-40] Airborne Hg passes a complex transformation cycle and acts as a global pollutant. Measurement of Hg content in the air of some industrial regions of China showed an increase in its levels in the range of 99.0-611 µg/m^3.[41] During the period from 2025 to 2030, the Hg emission limit should be reduced to 1 µg/m^3. To achieve this, alternative energy technologies, as well as measures on Hg elimination from the environment, must be developed and implemented.[42] Study of relevance between exposure of pregnant women to industrial air pollution with Hg in the United States and low birthweight in the offspring showed significantly positive odds ratios (aOR 1.04, 95% CI 1.02, 1.07).[43,44] In urbanized places where it is employed kerosene for cooking, aerial emission of pollutants, including heavy metals such as Hg, may affect household microenvironments, where women and children live daily. Women using kerosene showed enhanced cord blood levels of Hg and further heavy metals, besides to reduced vitamins such as B6 and folates ($P < 0.05$), and moreover, they were associated with a reduced newborn weight at the birth, an evidence reported after the correct adjustment of potential confounders ($\beta \pm$ standard error (SE) $= -0.326 \pm 0.155$; $P = 0.040$).[44]

2.2 | Mercury levels in the soil

The release of Hg from sources into the atmosphere can spread over long distances. Most of the environmental Hg, particularly in its ionic bivalent form, is localized at the site of matrix deposition and causes local environmental pollution.[42] To regulate the content of Hg in the soil, it is necessary to study its accumulation, distribution and sources. Soils of Chinese industrial regions have Hg content ranging from 310 to 3760 µg/kg.[43-45] Mercury concentration in rice ranged from 10 to 40 µg/kg, and 43% of the samples exceeded the regulatory limit value (20 mg/kg).[44] In anaerobic soils, there are conditions for the production of Hg which accumulates in rice and enters the human body through food chains. A significant increase of Hg concentration is found in drainage waters compared to irrigation waters in the ploughing season, which indicates the need to reduce the Hg concentration during this period.[46] Mercury contamination of soils is a great concern because of the Hg diffusion in groundwaters.[47] The possibility of contaminating soil-related components with heavy metals and Hg is, therefore, very frequently associated with the risk of Hg intake via raw food.[47-50]

2.3 | Mercury levels in blood and urine

Biomonitoring of the state of maternal and child health conducted in the framework of the COPHES/ DEMOCOPHES project reported that the Hg concentration in the urine of mothers living in the city was higher than in rural women.[27,51] Hg concentration in the mother's hair was higher than in children.[52] Its level increased in accordance with the number of dental amalgam fillings in the children, as well as the consumption of marine and fish products.[53] On average, the levels of Hg in the body of the screened persons did not exceed the recommended values.

A comparative analysis of Hg concentration in the blood of Canadian and Asian women entered to Canada over the past 5 years showed that biomarkers of Hg toxicants were found in higher concentrations in Asian women. This increased level of Hg in the immigrants was attributed to the consumption of seafood, dental amalgam fillings and the use of traditional medicines.[54]

3 | OCCUPATIONAL EXPOSURE TO MERCURY

3.1 | Inorganic mercury

Elemental Hg (metallic Hg^0), inorganic Hg salts and organic Hg compounds are three different chemical forms of Hg.[23] Elemental Hg (Hg^0) can be derived from old clinical thermometers, thermostats, latex paint and dental amalgams.[55-57] In the general population, dental amalgams represent the primary source of exposure to inorganic Hg.[58] Inorganic Hg (Hg salts) has been reported in teething powders, cosmetic products, antiseptics, diuretics and laxatives. It can also be induced from the elemental Hg vapour or MeHg metabolism.[59]

Although inorganic Hg salts have a low absorption when ingested, its vapour of elemental Hg^0 is accurately absorbed by the lungs and could be passed immediately into the brain through the blood-brain barrier.[60-62] Hg^0 has an important role in the global cycling of Hg and critical occupational health problems and is rapidly absorbed up to 80% by inhalation and crosses the blood-brain barrier, and intracellularly it is quickly oxidized to ionic Hg^{2+} which is retained.[23,62]

3.2 | Dental personnel

Dental personnel are among the professionals that are most exposed to Hg in their daily job practice. In many countries, dental personnel are still in their daily work exposed to a mixture of vapour of elemental Hg and inorganic Hg compounds. This is because of the administration of dental amalgam, which consists of 50% Hg.[54,63] Numerous studies have reported that dental personnel have notable higher mean levels of Hg in their blood samples compared to unexposed persons, especially in the older age group of dentists and dental assistants.[64-66] One study showed that 8% of dentists had higher hair Hg levels than 10 ppm, and 25% had a Hg level above 5 ppm.[59,63]

3.3 | Fluorescent lamp production

Workers in fluorescent lamp production are at risk of Hg exposure. Fluorescent lamps contain high amounts of Hg. The amount of Hg in a lamp varies from about 5 to 50 mg, depending on lamp size and the year of production. Newer lamps usually contain less than older lamps.[67] Only a few tenths of a milligram of Hg is required to maintain the vapour in a lamp. However, lamps must include more Hg to compensate for the part of Hg absorbed by internal parts of the lamp. And Hg-free lamps have considerably lower production of visible light, reduced to about half. Therefore, Hg is still considered an essential component of efficient fluorescent lamps. When a modern fluorescent tube is discarded, the main concern is the Hg, which is a significant toxic pollutant. One way to avoid releasing Hg into the environment is immediately to combine it with sulphur to form insoluble Hg sulphide, which will prevent vapour release. Some batteries also contain Hg that prevents the buildup of internal gases, although in recent years this use of Hg has declined.[20,68-74]

3.4 | Chloralkali workers

A significant relevance between the Hg concentration in the air and current contents in the blood of chloralkali workers has been established. The previous limit value for Hg in air 50 μg/m^3 corresponded to 30-35 μg/L in blood, however, with large deviations of values.[72] A comparative analysis of the excretion of Hg in the urine of chloralkali workers, residents of sea islands eating much fish and industrial workers not exposed to Hg showed that in the first group, the release of Hg was significantly higher (median value 15.4, range 4.8-35.0 μg/g creatinine) than in the control group (median value of 1.9, is 0.4-5.6 μg/g of creatinine) and in the inhabitants of the island (median value 6.5, range 1.8-21.5 μg/g creatinine).[75]

The study of chromosomal aberrations in the peripheral lymphocytes of male chloralkali workers exposed to Hg vapour revealed a slight increase in the chromosome and dicentric breaks in groups with a maximum level of Hg exposure or high cumulation of Hg.[76,77] Exposure to of Hg appeared to increase the level of total testosterone, presumably due to increased levels of the steroid-binding globulin (SHBG). However, for prolactin, cortisol and TSH, such a relationship was not detected.[78,79]

4 | ORGANIC MERCURY

The most important source of exposure to organic Hg in human beings seems to be the consumption of fish contaminated with MeHg.[80] Methylmercury is a bio-accumulative environmental toxicant, although minor behavioural and developmental effects of elemental Hg have been described at concentrations significantly lower than that required for comparable effects by MeHg.[81-83]

The many studies reviewed here found that organic Hg and Hg vapour have synergistic and independent developmental and toxic effects, along with those of other toxic metals, including nickel(Ni), palladium (Pd), gold (Au) and cadmium (Cd), and that additional conversions occur in the body between the different Hg forms.[84,85] Methylmercury, derived from fish, and dimethylmercury are readily absorbed in the gastrointestinal tract. MeHg is slowly demethylated and oxidized to Hg^{2+}.[86] Once assimilated into the cell, Hg2+ and MeHg+ form covalent bonds with glutathione and cysteine residues of proteins.[87] Organic Hg is found as the most frequent and most hazardous form of exposure to Hg that is frequently identified as EtHg and MeHg. It has been reported in different sources such as poultry, fish, fungicides, pesticides, insecticides and pharmaceutical preservatives. Although different data suggest that the most frequent exposure to MeHg should occur from fish consumption,[88,89] there are still people believing that exposure to EtHg may come from the administration of vaccines containing the preservative thimerosal that is quickly metabolized to this form, despite the many controversies on this issue.[90-94]

5 | MERCURY EXPOSURE AND FERTILITY: GENERAL ASPECTS

Mercury has a negative role in fertility, both in men and women.[95,96] In women, infertility is influenced by an imbalance of the female hormonal system due to Hg exposure. The progesterone/oestrogen ratio changes in favour of oestrogen growth, which inhibits the release of LH-luteinizing hormone. Thus, Hg may induce feminine infertility by increasing the prolactin secretion—analogous to the dopamine effect at the pituitary and midbrain level, with negative effects on galactopoiesis and female genitalia.[19,96] Xenobiotics such as Hg, xenoestrogens, and synthetic oestrogens are endocrine disruptors present in most commercial foods, plastic products, tap water, plastic water glass, cosmetics, cleaning products, clothes detergents, paints, pesticides and insecticides.[97] Careful identification and reducing of endocrine disruptors, including Hg exposures in everyday life, are essential to protect reproductive capacity. An analysis of the relevance between the concentration of toxic elements and reproductive health in women with reproductive disorders has reported that the probability of mature oocytes is oppositely proportional to the Hg concentration in the hair (RR = 0.81, 95% CI: 0.70-0.95).[98] The concentration of Hg in the hair of 30 subfertile women had a negative correlation with the formation of oocytes ($P < 0.05$) and the number of follicles ($P = 0.03$) after ovarian stimulation, while zinc and selenium levels had a positive relationship with these parameters.[99]

Mercury exposure has also been associated with polycystic ovary syndrome, premenstrual syndrome, dysmenorrhoea (menstrual pain), amenorrhoea, early menopause, endometriosis, benign breast disorders and galactorrhoea, often associated with female infertility. Numerous case reports have revealed adverse reproductive effects, although cause-effect relations are unproven, and safe exposure levels for Hg in the fecund women have not been documented.[100-102]

Studies have shown that reproductive effects such as developmental and infertility effects in the infants and foetus are at much lower contents and do not have any remarked effects on adults. Mercury, in its elementary form (Hg^0), as well as organic Hg, crosses the placental barrier and reaches the foetus, which can cause developmental defects.[103]

When compared to adults, the newborns and foetus show greater sensitivity to the effects of low contents of Hg exposure because of a less effective blood-brain barrier, higher rate of gastrointestinal absorption, less effective renal excretion and low body-weight with elevated food consumption rate per kilogram of body-weight.[63,104]

The study of the relationship between prenatal exposure to Hg and anthropometric characteristics of newborns conducted by Japanese scientists showed a negative relationship between the Hg concentration in the blood of mothers during the first and second trimester of pregnancy and the weight of children at birth ($r = -0.134$ and -0.119, respectively, $P < 0.05$). The mean values of Hg in the umbilical cord blood were twice as high as in the blood of mothers ($P < 0.001$). These results suggest that pregnant women and women of reproductive age should avoid even minimal contact with Hg because of its potentially adverse effects on foetal development.[105,106]

In the past, a study revealed that prenatal exposure to Hg at 16-18 weeks of gestation might cause accumulation of the Hg in the amniotic fluid and adversely affect the health status and children's cognitive skills since the children were approximately 3 years of age.[107] As already reported above, the main source of maternal Hg vapour exposure is amalgam fillings [54] and fish.[88,89] These two mercurials are known to penetrate the placenta rapidly and then pass into the foetus.

Foetal content of Hg after maternal inhalation was reported to be over 20-fold with respect to maternal exposure, which has been reported to be a similar dose of inorganic Hg,[108] and Hg contents in the heart, brain and main organs have been reported to be higher after equal levels to Hg vapour exposure are compared with the other Hg forms.[109,110]

Research in areas inhabited by the indigenous people of the Russian Arctic (from the Kola Peninsula to Chukotka) demonstrated the presence of both global and local sources of Hg pollution. Blood levels of Hg in women of reproductive age often exceed acceptable international levels.[111] The dose dependence of unfavourable outcome of the pregnancy and foetal development pathology (premature birth, low birthweight, miscarriages, stillbirths, congenital malformations) from mother exposure to Hg has been revealed. The average Hg levels in the blood of mothers with premature births, low birthweight, spontaneous abortions are 30% higher in comparison with unexposed women. A significantly increased relative risk of premature birth and birth of children with low body-weight and spontaneous abortions was found when the concentration of Hg exceeded 2 μg/L of plasma.[111]

As far as for the male reproductive health is concerned, even low-level exposure to Hg shows a negative impact (reduced semen quality and changes in sex hormone levels). A potential modifying or epigenetic effect of Hg on genetic polymorphism has been suggested, especially upon co-exposure with lead, cadmium and arsenic.[112] Exposure to Hg vapour induces accumulation of Hg in the testicles, where it exerts effects on the testicular steroidogenic and spermatogenic functions.[113] Daily administration of $HgCl_2$ to mice in a dose that did not affect body-weight caused a reduced sperm count, modified sperm morphology and lower fertility. It was possible to counteract this effect by administering vitamin E.[114] In vitro effect of $HgCl_2$ on Sertoli cells from rat was studied, revealing that concentrations <1 μmol/L of $HgCl_2$ significantly decreased the production of inhibin. Clinical observations have prompted suspicions of associations between acrodynia (pink disease) and obstructive epididymitis. However, good clinical data on the adverse effects of Hg on human spermatogenesis are still lacking.[57]

6 | INORGANIC MERCURY AND FERTILITY

The effect of Hg on fertility was investigated since the nineties, and the topic is to a limited extent updated by Berlin et al (2015).[57] Here, we will briefly review previous observations.

Rowland et al (1994) noted that exposure to elemental Hg vapour or inorganic Hg compounds might affect the fertility of laboratory animals.[115] Inhaled Hg vapour easily passes across the placenta to the foetus in human beings and leads to adverse effects on the developing foetus also by passing through the blood-brain barrier to the central nervous system.[64] Hg vapour released from amalgam to the blood of pregnant women rapidly passes the placenta and is recovered in foetal blood, pituitary gland and liver as well as in the amniotic fluid.[59,116] A significant correlation has been found between the Hg level in the infants, foetus, young children, as well as mother's milk and the number of amalgam fillings of the mother. The bioavailability of inorganic Hg could be increased in the breastmilk, which was reported to be excreted in milk from blood at a higher content in compared with the organic Hg.[116,117]

The binding to albumin is known as the main mechanism for Hg transferring. These studies were reported that dental amalgams could be the common source of Hg in the foetus and breastmilk for populations without high fish consumption and non-occupationally exposed populations, but significant contents of MeHg are also often reported in breastmilk.[108,116,118] It has been demonstrated that under normal Hg circumstances, the levels in mother's milk should be <1.7 μg/L according to the Agency for Toxic Substances and Disease Registry staff. This is to be a proper screening level for health problem.[119-121] Past reports have shown that in guinea pigs, rats, hamsters and mice exposed to inorganic Hg (1, 2 or 5 mg/kg/d intraperitoneally mercuric chloride for 1 month), the highest dosage induced cellular deformation of the Leydig cells and the seminiferous tubules and testicular degeneration in all species, whereas the lowest dosage induced testicular degeneration only in the hamster; partial degeneration was also reported in the mouse and rat, and no modification was observed in the guinea pig.[122] Declined levels of testosterone and testicular morphological changes were reported in rats orally exposed to mercuric chloride (9 mg/kg/d, for 60-180 days).[123] Decreased absolute degenerative testicular changes, and relative testicular weight, and decreased epididymal sperm count were reported in mice exposed to inorganic Hg by drinking water (4 ppm mercuric chloride, for 12 weeks). Also, a protective function of zinc was demonstrated.[124] Similar data were reported for human beings.[112] The administration of vitamin E, with mercuric chloride (1.25 mg/kg/d) through the gavage for 45 days in mice, showed a protective effect against decreased sperm motility, viability, epididymal sperm count and induced lower Hg content in the epididymis, vas deferens and testis.[114] Furthermore, many of these data have been recently confirmed.[125-127]

7 | OCCUPATIONAL EXPOSURE TO INORGANIC MERCURY AND FERTILITY

Some reproductive results, including reduced fertility, congenital abnormalities and spontaneous abortion, have been reported as a potential risk of Hg exposure in dental personnel.[59] For example, 81 women (45 dentists and 36 dental assistants) occupationally exposed to Hg were evaluated for reproductive hazards. The study revealed a significant correlation between hair Hg contents and the prevalence of menstrual cycle disorders.[128]

A past study with 103 male workers of zinc-mercury amalgam factory, who were exposed to elemental Hg vapour, revealed an average blood Hg contents of 14.6 μg/L. The outcome of this study reported no significant correlation between decreased fertility and Hg exposure.[129,130] Another study showed yet that 46 exposed pregnant women during exposure to inorganic Hg showed a higher frequency of congenital anomalies in offsprings.[131-133] The prevalence of reproductive system diseases among Chinese women working in industrial enterprises exposed to Hg reached 28.3%. The most common diseases were mammary hyperplasia, vaginitis and hysterioma (15.54%, 11.25% and 6.77%, respectively). A relationship between diseases of the reproductive system and exposure to Hg is established (OR = 1.452, 95% CI: 1.086-1.940).[134]

On the other hand, at paternal urinary Hg levels >4000 μg/L, an elevated rate of spontaneous abortions among workers exposed to Hg vapour was also reported, although the adverse effect was not significant after controlling for previous miscarriage history.[135] A trend of elevated rate of spontaneous abortions that were related to the paternal urinary Hg contents of 1-19 and 20-49 μg/L was reported in a study of exposed workers with Hg vapour [136,137]; however, the study did not report confounding factors, including alcohol consumption and smoking.

Industrial emission of Hg in Russia is 47 tons per year; the total amount of Hg-containing waste reaches 0.6-1 million tons. A screening of men working at mining enterprises in several Russian regions showed a reduction in erection and the quality of sexual acts, ejaculation and quality of orgasm. Investigation of spermatic fluid in 30 workers with an experience of more than 5 years who have not had children in marriage for more than 1 year (infertile marriage) demonstrated that only 33.5% of them had normal spermatogram parameters. In 28.5% of all cases, azoospermia and oligozoospermia of various degrees were detected (38%).[138]

8 | ORGANIC MERCURY AND FERTILITY

Exposure of mice to MeHg or inorganic Hg with single intraperitoneal injection of 1 mg Hg/kg body-weight confirmed adverse results on fertility, spermatogenesis and testicular morphology, whereas MeHg and, to a lesser extent, by inorganic Hg decreased the synthesis of DNA in spermatogonia.[139]

Intramuscular administration of MeHg to mice at doses 10-20 μg per day for 30 days leads to decrease in the mobility and number of spermatozoids, a violation of the tissue structure of the testes and a decline in the level of testosterone in the serum of male mice.[114] In monkeys exposed to MeHg (oral administration of 25 μg/kg/d for 20 weeks), decreased sperm motility and increased abnormal sperm tail morphology were observed at subneurotoxic levels; there was no modification in serum testosterone and testicular morphology.[140,141] In rats exposed to MeHg with 0.8, 8.0 or 80 μg/kg twice weekly in the diet for 19 weeks, somewhat declined epididymal sperm count and markedly lowered intratesticular testosterone were reported in the group with high dose of MeHg, whereas inverse relevance was noted between testicular Hg content and fertility.[142] Experimental studies indicate that the addition of MeHg to fish food at doses of 0.87-3.93 micrograms decrease their reproductive function. There was a decrease in testosterone levels in males of fish and oestrogen in females, and a slowdown in the development of gonads in females.[143]

In contrast, researchers from the United States who studied the reproductive effects of Hg on pairs of mallards observed that MeHg added to the feed at a dose of 0.5 μg/g, resulted in successful incubation of eggs significantly higher than in controls (71.8% and 57.5%, respectively), the average number of ducklings per female also exceeded the control rate (21.4 and 16.8, respectively), their weight was significantly higher (87.2 g and 81.0 g, respectively). These results suggest a possible hormesis effect for small doses of Hg.[144]

Since MeHg can pass the blood-brain barrier, it affects the brain, and the foetal brain is evaluated to be the critical organ. MeHg easily passes across the placental barrier from mother to foetus, thereby increasing the risk of mental retardation and motor disturbance.[145,146] A study of the effect of MeHg in doses from 1 to 100 nM on the zebrafish organism in three generations has shown the correlation of anomalous neurobehavioural status (including hyperactivity and visual deficit) with sperm epimutations in the F2 generation of adult zebrafish. This allows us to assume that exposure to MeHg can contribute to the epigenetic inheritance of diseases not only in zebrafish (an established human health model) but in all species, including human beings.[147]

A study of Japanese scientists conducted in the residents of Minamata City exposed to Hg in the 1950s-1960s reported elevated levels of spontaneous stillbirth and fertility compared with an unexposed population ($P < 0.001$). There was an elevated report in the male proportion among stillbirths, which corresponded to a decrease in the proportion of men at birth in the late 1950s.[148] An investigation of the association between fish consumption, Hg content in the hair and sperm parameters among 129 men attending reproductive centres found that an increase in the Hg level in the hair had a direct relationship with the sperm concentration, the total number of spermatozoa and their progressive mobility, taking into account the influence of age, index body-weight, smoking and alcohol drinking. This relevance was greater among men who had fish consumption higher than the average in the population. The volume of the seed and normal morphology were not related to the Hg contents in the hair.[149]

9 | CONCLUDING REMARKS

Numerous literature data analysed in this MiniReview indicate negative effects of both organic and inorganic elemental Hg in relation to fertility, reproductive health and pregnancy outcome. Most of the analysed literature referred to experiments on animals, birds and fish due to the difficulty of doing such studies in human beings. Exposure to inorganic or elemental Hg mainly occurs in professional groups, such as dental stuff, industrial workers producing thermometers, thermostats, dental amalgams and chloralkali workers. Methylmercury enters the human body with fish through the food chains. An example of Hg exposure is the Minamata disease. The cause of the disease was the prolonged release of inorganic Hg into the water of Minamata Bay, which was converted by the microorganisms to MeHg.

The effects of Hg on the reproductive function of human beings are manifested in both men and women. Mercury can alter the shape, movement of sperm and decrease its quantity and quality. In men exposed to Hg, a reduction in erection, quality of sexual acts and ejaculation was found. Research indicates that Hg influences the levels and function of oestrogen and reduces fertility in women. Mercury exposure has a relation with the polycystic ovary syndrome, premenstrual syndrome, dysmenorrhoea, amenorrhoea, premature menopause, endometriosis, benign breast disorders and abnormal lactation. In pregnant women, Hg passes through the placental membrane, which can cause spontaneous abortions, premature births, congenital disabilities and retardation of foetus development.

Future perspectives involve research to prevent risk factors for congenital anomalies and identify risk factors. Abandoning the use of dental amalgam, which is the essential source of Hg vapour exposure in the general population, would be an important international measure in the decrease of Hg exposure.

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