Vol. 12. No.3. 2023

DOI: 10.13140/RG.2.2.27283.25124

Contents available at:

http://www.crdeepjournal.org

International Journal of Environmental Sciences (ISSN: 2277-1948) (SJIF Value: 6.04)
UGC Approved-A Peer Reviewed Quarterly Journal

Review Paper

Impact of Mercury on Health: A Comprehensive Review on its Consequences

Dr. G. Tirumalavasu Deva Rao[1] and Dr. G. Swathi[2]

[1].*Lecturer in Social studies, IASE Government B.ED College, Nellore, India.*
[2]*Assistant Professor in Zoology, Government degree college, Nagari, India.*

ARTICLE INFORMATION

Corresponding Author:
G. Tirumalavasu Deva Rao

Article history:
Received: 02-09-2023
Revised: 04-09-2023
Accepted: 14-09-2023
Published: 19-09-2023

Key words:
Mercury, Health, Consequences, Toxicity, Pollution

ABSTRACT

Mercury pollution is an ancient problem that has evolved into a global environmental concern. This comprehensive review examines the impact of mercury on health and explores the various consequences of its exposure. The review covers both historical and modern perspectives, encompassing the origins of mercury pollution, its role in industrial processes, and its widespread distribution in the environment. The review highlights the studies in Minamata tragedy, which brought global attention to the neurological and developmental effects of mercury poisoning. Regarding human health, the review covers a wide range of consequences, including neurological disorders, liver damage, cardiovascular effects, and reproductive issues. In conclusion, this comprehensive review highlights the urgent need for continued research, international collaboration, and stringent regulatory measures to mitigate the health consequences of mercury pollution. Understanding the health impacts of mercury pollution is crucial for implementing effective strategies to protect both humans and the environment from this hazardous metal.

Introduction

Mercury is a naturally occurring element that is released into the environment through both natural processes and human activities. However, human activities, particularly industrial processes, have significantly increased the amount of mercury in the environment, leading to widespread pollution. Mercury pollution has a long history that spans several centuries. Mercury has been used in various applications throughout history due to its unique properties. Some common uses include the production of thermometers, barometers, electrical switches, fluorescent lamps, dental amalgams, and certain batteries. It has also been used in industrial processes, such as gold and silver mining, and as a catalyst in chemical reactions (IARC, 1993).

Mercury is extremely toxic to all living organisms in the environment. Its vapors can be inhaled and absorbed through the lungs, while ingesting mercury compounds or contaminated food can lead to poisoning. Mercury exposure can cause severe health effects, particularly on the nervous system, kidneys, and cardiovascular system. Developing fetuses and young children are particularly vulnerable to the harmful effects of mercury. Mercury exists in various forms: elemental and inorganic (where people might be exposed through their occupation); and organic (e.g., methyl mercury) (Harda, 1978). These forms of mercury differ in their degree of toxicity and in their effects on all the nervous, digestive and immune systems, and on lungs, kidneys, skin and eyes (Bridges and Zalups, 2010). Mercury occurs naturally in the earth's crust. It is released into the environment through natural process like volcanic activity, weathering of rocks and also by the result of human activity. Human activity plays a main role in mercury release, as from coal-fired power stations, coal burning for heating and cooking, industrial processes, waste incinerators and as a result of mining for mercury, gold and other metals.

Mercury is a persistent pollutant that can accumulate in the environment and the food chain. It can be released into the air, water, and soil through natural processes, but human activities, such as coal combustion, industrial emissions, and improper disposal of mercury-containing products, are significant contributors to environmental mercury pollution. Once released, mercury can be transformed into methyl mercury, a highly toxic and bioaccumulative form that can concentrate in fish and other organisms. Due to the significant

health (Cortes et al., 2018) and environmental risks associated with mercury, there have been international efforts to regulate and control its use and emissions. Public awareness and responsible management of mercury are essential for protecting human health and the environment from its harmful effects.

Here is an overview of the history of mercury pollution. Early civilizations, such as the Egyptians and Chinese, used it for medicinal and cosmetic purposes. The review starts with an introduction to the element's history and its increasing use in industrial processes during the modern era.

Mercury history

Mercury, also known as quicksilver, is one of the few elements that have been known since ancient times. Its discovery is not attributed to a single individual because it has been used and recognized by various civilizations throughout history.The ancient Egyptians and Chinese are believed to have known about mercury as early as 1500 BCE. They used it for medicinal and cosmetic purposes and likely discovered it in its natural form.The Greek philosopher Theophrastus described the process of extracting mercury from cinnabar (mercury sulfide) around 300 BCE. Theophrastus was a student of Aristotle and one of the early pioneers in studying minerals and metals. In terms of the element's name "mercury," it has its roots in Roman mythology. The Romans associated the element with the god Mercury, who was the messenger of the gods and the god of trade, profit, and commerce. The reason behind this association is likely due to the element's unique physical properties and its use in various trade-related applications.

It is important to note that while mercury was known and used by ancient civilizations, it wasn't until much later in history that the understanding of its properties and its role in various processes advanced significantly. Today, we have a much better understanding of the element and its potential environmental and health risks, which has led to more stringent regulations to limit its use and release into the environment (Jones, 1999).

Early Industrial Era (19th and early 20th centuries): During the early stages of the Industrial Revolution, mercury was extensively used in various industries. It was used in the production of chlorine and caustic soda, as well as in the extraction of gold and silver from ores. These processes resulted in the release of large quantities of mercury into the air and water bodies. The impacts of mercury pollution were not well understood at the time, and little attention was given to its environmental consequences. Romans used vermillion (the red-colored sulfur salt of mercury) extracted from the Almadén cinnabar mines as a cosmetic and decorative (Goldwater, 1972).

Mid-20th Century: In the mid-20th century, the detrimental effects of mercury pollution started to become apparent. One of the most notorious incidents of mercury poisoning occurred in Minamata, Japan, in the 1950s and 1960s. The Chisso Corporation, a chemical company, released methyl mercury, a highly toxic form of mercury, into Minamata Bay. The mercury bio accumulated in fish and shellfish, which were then consumed by the local population. Thousands of people suffered from mercury poisoning, leading to severe neurological damage and deaths. The Minamata incident raised global awareness about the dangers of mercury pollution.

Mercury levels

Under the Safe Drinking Water Act, EPA in 1991 set an enforceable regulation for inorganic mercury, called a maximum contaminant level (MCL), at 0.002 mg/L or 2 ppb. As per WHO standards of mercury levels were 0.001 mg/l, for drinking water and 0.01 mg/l, for industrial effluents.

Impact of Mercury pollution on Health

Mercury pollution can cause various health problems and diseases, particularly when humans are exposed to high levels of mercury over a prolonged period. The toxicity of mercury depends on its form, with methylmercury being the most dangerous to human health. Here are some diseases and health effects associated with mercury pollution:

1. Minamata Disease: Minamata disease is one of the most well-known examples of mercury poisoning. It occurred in the 1950s and 1960s in Minamata, Japan, due to the consumption of seafood contaminated with methylmercury (Harda, 1978). Symptoms include neurological damage, numbness, muscle weakness, impaired vision and hearing, tremors, and in severe cases, paralysis, coma, and death (Nagaki J, 1985;Sakamoto et al., 2018; NRC, 2000; UNIDO, 2008; Takeuchi and Eto, 1999; Nishigaki and Harada, 1975; Tokuom et al., 1961).
2. Neurological Disorders: Mercury has a strong affinity for the nervous system and can cause various neurological disorders (Hussain et al. 1997, Letz et al. 2000; Yin et al, 2011). High levels of mercury exposure, especially in developing fetuses and young children, can lead to impaired cognitive function, learning disabilities, and developmental delays (Pinheiro et al 2008; Coxet al.1989). It may also cause tremors, memory loss, irritability, and other behavioral changes in adults. Mercury toxicity leads to neurodegenerative effects (Carocci et al. 2014, Houston, 2011). Mercury exposure leads to oxidative stress (Teixeira et al.2018) in order causing array of illness like Epilepsy, Parkinson's disease, Alzheimer's disease (Bridges CC, Zalups, 2010; Roulet et al. 1998; Szász et al., 2002)
3. Cardiovascular Effects: Chronic exposure to mercury has been linked to cardiovascular diseases (Fernandes et al. 2012). It can damage blood vessels, increase blood pressure, hypertension (Carmignani et al. 1992; Wakita et al. 1987; Houston et al. 2007) and affect the functioning of the heart muscle (Vassallo et al. 1999; Da Cunha et al., 2000; Omanwar et al., 2011,

2013). Studies have shown that long-term mercury exposure may contribute to an increased risk of heart attacks, heart disease, and stroke (Genchi et al. 2017, Oliveira et al. 1994).

4. Liver damage:In severe cases, prolonged exposure to high levels of inorganic mercury can lead to liver failure (Trebucobich et al., 2014; Choi et al., 2017) and also decline in liver enzyme functions (Futatsuka et al., 1992; Lee et al., 2014; Lee et al., 2017). Animal studiesshowed necrotic changes were observed in most of the liver tissue samples upon a histological examination (Wadaan, 2009; 5. Macirella et al., 2016; Ung et al., 2010)
5. Renal Damage: Mercury can cause damage to the kidneys, leading to impaired kidney function. Prolonged exposure to mercury may result in kidney dysfunction, failure, proteinuria (presence of protein in urine), and even renal injury or nephropathy (Ha et al. 2016, Pollack et al, 2015, Li SJ et al. 2010, Carranza-Rosales et al. 2005, Habiba et al. 2016, MananDoshi et al. 2009, Yawei et al. 2021).Mercury accumulates in proximal tubular cells(Aslamkhan et al. 2003). ZhenzhenGao, et al., 2022 showed that due to chronic mercury poisoning causesnephrotic syndrome. Typical sclerotic glomeruli with expanded mesangial matrix, shrinkage and occlusion of the glomerular capillaries (Bridges et al. 2014,Denic et al. 2016). There were numerous intracellular and intercellular enzymes detected in urine (Stacchiotti et al. 2009, Prozialeck and Edwards 2010, Zalups 2000, Kanda et al. 2008, Al Bakheet et al. 2013, Bridges et al. 2013,Agrawal et al. 2014,Carneiro et al. 2014, Joshi et al. 2014a, 2014b) and also excretion of Hg in the urine (Engstrom et al. 2013) . Animal studies showed that there is Hg-mediated nephrotoxicity (Bridges et al. 2014, Zalups et al. 2014, Hazelhoff et al. 2021, Goel et al. 2023).
6. Reproductive and Developmental Effects: Mercury can have adverse effects on reproductive health and development (El-Desoky et al., 2013; Kalender et al., 2013; Henriqueset al., 2019; Kumar et al., 2022). In pregnant women, high levels of mercury exposure can lead to developmental abnormalities in the fetus, including neurological impairments (Solan and Lindow, 2014). It can also impact fertility and increase the risk of miscarriages (Panet al., 2007; Rodríguez-Villamizaret al., 2015; Maeda et al., 2018; Sukhn et al., 2019; Bjorklund et al., 2019).
7. Respiratory Problems: Inhalation of mercury vapor can cause respiratory problems, particularly in occupational settings where mercury is used or released (Smiechowicz et al., 2017). Chronic exposure to mercury vapor may lead to respiratory inflammation, bronchitis, and lung damage (Lilis et al., 1985; Linet al., 1989; Rowens et al., 1991 Asano et al., 2000; Moromisato et al., 1994; Kanluenand Gottlieb, 1991, Cortes et al., 2018).

It is important to note that the severity of these health effects depends on the dose, duration, and route of exposure to mercury. Minimizing exposure to mercury and implementing strict environmental regulations are essential for preventing mercury-related diseases and protecting human health.

Regulatory Measures and Awareness (1970s-1990s): In response to growing concerns about mercury pollution, various countries began implementing regulations to control its release into the environment. The United States passed the Clean Air Act in 1970, which targeted reductions in air pollution, including mercury emissions. The use of mercury in industrial processes started to decline, and efforts were made to improve waste management and treatment practices.

International Actions: The global community recognized the need for concerted efforts to address mercury pollution. In 1990, the United Nations Environment Programme (UNEP) initiated the Global Mercury Assessment Program to assess the global impact of mercury pollution. This program led to the establishment of the Intergovernmental Negotiating Committee on Mercury (INC) in 2003, which aimed to develop a legally binding instrument on mercury. After years of negotiations, the Minamata Convention on Mercury was adopted in 2013 and entered into force in 2017. The convention seeks to control mercury emissions and reduce its use in various industries.

Current Challenges and Future Outlook: Although significant progress has been made in reducing mercury pollution, challenges remain. Artisanal and small-scale gold mining, coal-fired power plants, and industrial processes still contribute to mercury emissions. Mercury can travel long distances through the atmosphere, leading to global distribution and contamination of ecosystems far from the original sources. Mercury accumulates in the food chain, particularly in fish and seafood, posing risks to human health.
Efforts are ongoing to further regulate mercury use and emissions, promote cleaner technologies, and increase public awareness. Continued research, monitoring, and international collaboration are crucial to addressing the challenges posed by mercury pollution and minimizing its adverse impacts on human health and the environment.

Conclusion

Industrialization brought human progress today, with consequently had the side effects of pollution which both are inevitable. We need sustainable scientific approaches to balance this scenario.The review concludes with a summary of the mercury pollution, emphasizing the lessons learned and the urgency of continued efforts to protect the environment and human health from this enduring threat.

References

Agrawal, S., Flora, G., Bhatnagar, P., and Flora, S.J.(2014). Comparative oxidative stress, metallothionein induction and organ toxicity following chronic exposure to arsenic, lead and mercury in rats. Cell Mol.Biol., 60(2):13–2.

Al,Bakheet, S.A., Attafi, I.M., Maayah, Z.H., Abd-Allah, A.R., Asiri, Y.A., and Korashy, H.M.(2013). Effect of long-term human exposure to environmental heavy metals on the expression of detoxification and DNA repair genes. Environ. Pollut, 181: 226–232. 10.1016/j.envpol.2013.06.014

Asano, S., Eto, K., Kurisaki, E., Gunji, H., Hiraiwa, K., Sato, M., Sato, H., Hasuike, M., Hagiwara, N., Wakasa, H. 2000. Acute inorganic mercury vapor inhalation poisoning. Pathol Int. Mar;50(3):169-74. https://doi.org/10.1046/j.1440-1827.2000.01032.x

Aslamkhan, A.G., Han, Y.H., Yang, X.P., Zalups, R.K., and Pritchard. J.B. 2003. Human renal organic anion transporter 1-dependent uptake and toxicity of mercuric-thiol conjugates in Madin-Darby canine kidney cells. Mol. Pharmacol, 63(3):590-6. https://doi.org/10.1124/mol.63.3.590

Beryllium, Cadmium, Mercury, and Exposures in the Glass Manufacturing Industry, 1993; International Agency for Research on Cancer (IARC), Working Group on the Evaluation of Carcinogenic Risks to Humans, which met in Lyon, 9–16 February 1993

Bjørklund, G., Chirumbolo, S., Dadar M., Pivina, L., Lindh, U., Butnariu, M., Aaseth, J. 2019. Mercury exposure and its effects on fertility and pregnancy outcome. Basic ClinPharmacolToxicol, 125(4):317-327. **https://doi.org/10.1111/bcpt.13264**

Bridges, C.C, Zalups, R.K. 2010. Transport of inorganic mercury and methylmercury in target tissues and organs. Journal of Toxicology and Environmental Health—Part B,13(5):385–410. https://doi.org/10.1080/10937401003673750

Bridges, C.C., Joshee, L., and Zalups, R.K. 2014. Aging and the disposition and toxicity of mercury in rats. Exp. Gerontol, 53: 31–39. https://doi.org/10.1016/j.exger.2014.02.006

Bridges, C.C., Joshee, L., van den Heuvel, J.J., Russel, F.G., and Zalups, R.K. 2013. Glutathione status and the renal elimination of inorganic mercury in the Mrp2($^{-/-}$) mouse. PLoS One, 8(9): e73559.https://doi.org/10.1371/journal.pone.0073559

Carmignani, M., Boscolo, P., Artese, L., Del Rosso, G., Porcelli, G., Felaco, M., Volpe, A.R., Giuliano G.1992. Renal mechanisms in the cardiovascular effects of chronic exposure to inorganic mercury in rats. British Journal of Industrial Medicine, 49(4):226–232. http://dx.doi.org/10.1136/oem.49.4.226

Carneiro, M.F., Grotto, D., and Barbosa,Jr.,F. 2014. Inorganic and methylmercury levels in plasma are differentially associated with age, gender, and oxidative stress markers in a population exposed to mercury through fish consumption. J. Toxicol. Environ. Health A,77(1-3):69-79. https://doi.org/10.1080/15287394.2014.865584

Carocci, A., Rovito, N.,Sinicropi, M.S., and Genchi, G. 2014. Mercury toxicity and neurodegenerative effects. Rev. Environ. Contam. Toxicol, 229: 1–18. https://doi.org/10.1007/978-3-319-03777-6_1

Carranza-Rosales, P., Said-Fernandez, S., Sepulveda-Saavedra, J., Cruz-Vega, D.E., and Gandolfi, A.J. 2005. Morphologic and functional alterations induced by low doses of mercuric chloride in the kidney OK cell line: Ultrastructural evidence for an apoptotic mechanism of damage. Toxicology, 210 (2-3):111-21. https://doi.org/10.1016/j.tox.2005.01.006

Cavalleri A, Gobba F. (1998)Reversible colour vision loss in occupational exposure to metallic mercury. *Environ Res*,1998;77(2):173–177.10.1006/enrs.1997.3814.

Choi, J., Bae, S., Lim, H., Lim, J.A., Lee, Y.H., Ha, M., Kwon, H.J. 2017. Mercury Exposure in Association With Decrease of Liver Function in Adults: A Longitudinal Study. J Prev Med Public Health, 50(6):377-385. https://doi.org/10.3961/jpmph.17.099.

Cortes, J., Peralta, J., DíazNavarro, R. 2018. Acute respiratory syndrome following accidental inhalation of mercury vapor. Clin Case Rep,6(8): 1535–1537.

Cox, C., Clarkson, T.W., Marsh, D.O., Amin-Zaki, L., Tikriti, S., Myers, G.G. 1989. Dose-response analysis of infants prenatally exposed to methyl mercury: an application of a single compartment model to single-strand hair analysis. Environmental Research, 49(2):318–332. https://doi.org/10.1016/S0013-9351(89)80075-1

Da Cunha,V.,Souza, H. P., Rossoni, L. V., França, A. S., Vassallo, D. V. 2000. Effects of mercury on the isolated perfused rat tail vascular bed are endothelium- dependent. Archives of Environmental Contamination and Toxicology,39(1):124-30. https://doi.org/10.1007/s002440010001

Denic, A., Glassock, R.J., and Rule, A.D. 2016. Structural and functional changes within the aging kidney. Adv. Chronic Kidney Dis, 23(1):19-28. https://doi.org/10.1053/j.ackd.2015.08.004

El-Desoky, G. E., Bashandy, S. A., Alhazza, I. M., Al-Othman, Z. A., Aboul-Soud, M. A., Yusuf, K. (2013). Improvement of mercuric chloride-induced testis injuries and sperm quality deteriorations by *Spirulinaplatensis* in rats. PLoS One, 8(3):e59177. https://doi.org/10.1371/journal.pone.0059177

Engstrom K.,Ameer S.,Bernaudat L, Drasch G, Baeuml J, Skerfving S, Bose-O'Reilly S, and Broberg K 2013. Polymorphisms in genes encoding potential mercury transporters and urine mercury concentrations in populations exposed to mercury vapor from gold mining. Environ. Health Persp, 121(1): 85–91. https://doi.org/10.1289/ehp.1204951

FernandesAzevedo B, Barros Furieri L, Peçanha FM, Wiggers GA, FrizeraVassallo P, RonacherSimões M, Fiorim J, Rossi de Batista P, Fioresi M, Rossoni L, Stefanon I, Alonso, M.J., Salaices, M., Valentim,Vassallo, D.2012. Toxic effects of mercury on the cardiovascular and central nervous systems. J Biomed Biotechnol, 2012:949048. doi: 10.1155/2012/949048

Futatsuka, M., Kitano, T., Nagano, M., Inaoka T., Arimatsu Y., Ueno T., Wakamiya, J., Miyamoto, K. 1992. An epidemiological study with risk analysis of liver diseases in the general population living in a methyl mercury polluted area. J Epidemiol Community Health. 1992:46(3):237–240. doi: 10.1136/jech.46.3.237

Genchi, G, Sinicropi, M.S., Carocci, A., Lauria, G., Catalano, A. 2017. Mercury Exposure and Heart Diseases. Int J Environ Res Public Health, 14(1):74. doi: 10.3390/ijerph14010074

Gochfeld, M. 2005. Chronologic history of occupational medicine. J Occup Environ Med, 47(2):96-114. doi: 10.1097/01.jom.0000152917.03649.0e

Goel, H., Printz, R.L., Shiota, C., Estes, S.K., Pannala,, V., AbdulHameed, M.D.M., Shiota, M., Wallqvist, A. 2023. Assessing Kidney Injury Induced by Mercuric Chloride in Guinea Pigs with In Vivo and In Vitro Experiments. International Journal of Molecular Sciences, 24(8):7434. doi:10.3390/ijms24087434.
Gritzka, T.L., and Trump, B.F. 1968. Renal tubular lesions caused by mercuric chloride. Electron microscopic observations: degeneration of the pars recta. Am. J. Pathol. 52(6): 1225–1277.
Ha, E., Basu, N., Bose-O'Reilly, S., Dorea, J.G., McSorley, E., Sakamoto, M., and Chan H.M. 2016. Current progress on understanding the impact of mercury on human health. Environ Res, 152:419-433. doi: 10.1016/j.envres.2016.06.042
Habiba, G.,Abebe, G., Bravo, A.G.,Ermias, D.,Staffan A., and Bishop, K. 2016. Mercury human exposure in populations living around Lake Tana (Ethiopia). Biol. Trace Elem. Res, doi: 10.1007/s12011-016-0745-9.
Harada M. 1978. Congenital minamata disease: Intrauterine methylmercury poisoning. Teratology, 18:285–288. doi: 10.1002/tera.1420180216.
Hazelhoff, M.H.,Bulacio, R.P., Torres, A.M. 2021. Trimetazidine Protects from Mercury-Induced Kidney Injury. Pharmacology, 106(5-6):332-340. doi: 10.1159/000514843
Henriques, M.C.,Loureiro, S.,Fardilha, M.,Herdeiro, M.T.2019. Exposure to mercury and human reproductive health: A systematic review. ReprodToxicol, 85:93–103. doi: 10.1016/j.reprotox.2019.02.012
Houston, M.C. 2011. Role of Mercury Toxicity in Hypertension, Cardiovascular Disease, and Stroke. J. Clin. Hyperten,13:621–627. doi: 10.1111/j.1751-7176.2011.00489.x.
Houston, M.C.2007. The role of mercury and cadmium heavy metals in vascular disease, hypertension, coronary heart disease, and myocardial infarction. Alternative Therapies in Health and Medicine. 13(2):S128–S133.
https://doi.org/10.1002/ccr3.1656
https://www.nhm.ac.uk/discover/planet-mercury.html
Hussain, S., Rodgers, D.A., Duhart, H.M., Ali, S.F. 1997. Mercuric chloride-induced reactive oxygen species and its effect on antioxidant enzymes in different regions of rat brain. J. Environ. Sci. Health B. 32:395–409. doi: 10.1080/03601239709373094.
Jones DW. Exposure or absorption and the crucial question of limits for mercury. J Can Dent Assoc. 1999 Jan;65(1):42-6. PMID: 9973766.
Joshi D., Kumar M.D., Kumar S.A., and Sangeeta S. 2014a. Reversal of methylmercury-induced oxidative stress, lipid peroxidation, and DNA damage by the treatment of N-acetyl cysteine: a protective approach. J. Environ. Pathol. Toxicol. Oncol, 33(2):167–182. doi: 10.1615/jenvironpatholtoxicoloncol.2014010291
Joshi D., Mittal D.K.,Shukla S.,Srivastav A.K., and Srivastav S.K. 2014b. N-acetyl cysteine and selenium protects mercuric chloride-induced oxidative stress and antioxidant defense system in liver and kidney of rats: A histopathological approach. J. Trace Elem. Med. Biol, 28: 218–226.
Kalender, S., Uzun, F. G., Demir, F., Uzunhisarcıkli, M., Aslanturk, A. (2013). Mercuric chloride-induced testicular toxicity in rats and the protective role of sodium selenite and vitamin E. 55 456–462. doi:10.1016/j.fct.2013.01.024
Kanda, H.,Kikushima, M., Homma-Takeda, S.,Sumi, D., Endo, A., Toyama, T., Miura, N.,Naganuma, A., and Kumagai, Y. 2008. Downregulation of arginase II and renal apoptosis by inorganic mercury: Overexpression of arginase II reduces its apoptosis. Arch. Toxicol, 82(2):67-73. doi: 10.1007/s00204-007-0244-z
Kanluen, S., Gottlieb, C.A.1991. A clinical pathologic study of four adult cases of acute mercury inhalation toxicity. Arch Pathol Lab Med, 115(1):56–60.
Kumar, S., Sharma, A.,Sedha, S. 2022. Occupational and environmental mercury exposure and human reproductive health - a review. J Turk GerGynecolAssoc, 23(3):199-210. doi: 10.4274/jtgga.galenos.2022.2022-2-6
Lee, H., Kim, Y.,Sim, C.S., Ham, J.O., Kim, N.S., Lee, B.K.2014. Associations between blood mercury levels and subclinical changes in liver enzymes among South Korean general adults: analysis of 2008-2012 Korean National Health and Nutrition Examination Survey data. Environ Res, 130:14-9. doi: 10.1016/j.envres.2014.01.005.
Lee, M.R., Lim, Y.H., Lee, B.E., Hong, Y.C. 2017. Blood mercury concentrations are associated with decline in liver function in an elderly population: a panel study. Environ Health, 16(1):17. doi: 10.1186/s12940-017-0228-2
Leonard J, Goldwater. 1972. Mercury: A History of Quicksilver, York Press, First Edition. Baltimore, MD,xi, 318 p.
Letz, R.,Gerr, F.,Cragle, D.,Green, R.C., Watkins, J.,Fidler, A.T. 2000.Residual neurologic deficits 30 years after occupational exposure to elemental mercury. Neurotoxicology, 21(4):459-74.
Li, S.J., Zhang, S.H., Chen, H.P., Zeng, C.H.,Zheng, C.X., Li, L.S., Liu Z.H. 2010. Mercury-induced membranous nephropathy: clinical and pathological features. Clin J Am SocNephrol,5(3):439-44. doi: 10.2215/CJN.07571009.
Lilis, R., Miller, A.,Lerman, Y. 1985. Acute mercury poisoning with severe chronic pulmonary manifestations. Chest, 88(2): 306–309.

Lin, T.C.,Gue, Z.W., Hwang, M.S. 1989. Acute pneumonitis caused by inhalation of mercury vapor – report of a case. Zhonghua Yi XueZaZhi,43(2): 141–146.
Macirella R., Guardia A., Pellegrino DV., Bernabò I.,Tronci V., Ebbesson LO.,Sesti, S., Tripepi, S., Brunelli, E.2016. Effects of two sublethal concentrations of mercury chloride on the morphology and metallothionein activity in the liver of zebrafish (Daniorerio) Int J MolSci, 17(3):361. doi: 10.3390/ijms17030361
Maeda E, Murata K, Kumazawa Y, Sato W, Shirasawa H, Iwasawa T, Izumo K, Tatsuta N, Sakamoto M, Terada Y. 2019. Associations of environmental exposures to methylmercury and selenium with female infertility: a case-control study. Environ Res, 168:357-363. doi: 10.1016/j.envres.2018.10.007

Manan,Doshi., Rajeev, A.,Annigeri, Prakash, C.,Kowdle, SubbaRao,Budithi.,MahendranVarman. 2019. Membranous nephropathy due to chronic mercury poisoning from traditional Indian medicines: report of five cases, Clinical Kidney Journal, 12 (2) Pages 239–244, doi:10.1093/ckj/sfy031

Moromisato, D.Y.,Anas, N.G., Goodman, G. 1994. Mercury inhalation poisoning and acute lung injury in a child. Use of high-frequency oscillatory ventilation. Chest.105(2): 613–615.

Nagaki, J., Ohnishi, A., Kuroiwa, Y.1985.Electrophysiologic and histopathologic studies on sural nerves from Minamata disease patients of delayed onset showing distal sensory impairments. RinshoShinkeigaku, 25:88-94.

Nishigaki, S., Harada, M. 1975. Methylmercury and selenium in umbilical cords of inhabitants of the minamata area. Nature. 1975;258:324–325. doi: 10.1038/258324a0.

NRC (National Research Council) Toxicological Effects of Methylmercury. Academic Press; Washington, DC, USA: 2000.

Oliveira, E.M., Vassallo, D.V., Sarkis, J.J.F., Mill J.G. 1994. Mercury effects on the contractile activity of isolated heart muscle. Toxicol. Appl. Pharmacol, 128:86–91. doi: 10.1006/taap.1994.1183.

Omanwar, S., Ravi, K., Fahim, M. 2011. Persistence of EDHF pathway and impairment of the nitric oxide pathway after chronic mercury chloride exposure in rats: mechanisms of endothelial dysfunction. Hum ExpToxicol, 30(11):1777-84. doi: 10.1177/0960327110391389

Omanwar, S., Saidullah, B., Ravi, K., Fahim, M. 2013. Vasorelaxant effects of mercury on rat thoracic aorta: the nitric oxide signaling mechanism. Hum ExpToxicol, 33(9):904-10. doi: 10.1177/0960327113512341

Pan, J., Song, H., Pan, X.C. 2007. Reproductive effects of occupational exposure to mercury on female workers in China: a meta-analysis. Zhonghua Liu Xing Bing XueZaZhi, 28(12):1215-8.

Pinheiro, M.C.N.,Crespo-López,M.E.,Vieira, J.L.F., Oikawa, T.,Guimarães, G.A.,Araújo, C.C.,Amoras, W.W., Ribeiro, D.R., Herculano, A.M., Nascimento, J.L.M.,Silveira, L.C.L. 2008. Mercury pollution and childhood in Amazon riverside villages. Environment International. 33(1):56-61. doi: 10.1016/j.envint.2006.06.024

Pollack, AZ., Mumford, S.L,Mendola, P., Perkins, N.J., Rotman, Y.,Wactawski-Wende, J., and Schisterman, E.F., 2015. Kidney biomarkers associated with blood lead, mercury, and cadmium in premenopausal women: A prospective cohort study. J Toxicol Environ Health A, 78(2):119-31. doi: 10.1080/15287394.2014.944680

Prozialeck, W.C., and Edwards, J.R. 2010. Early biomarkers of cadmium exposure and nephrotoxicity. Biometals, 23(5):793-809. doi: 10.1007/s10534-010-9288-2

Riva,M.A., Sironi, V.A., Fano, D., Cesana, G. 2011. Workers' health conditions in the Greco-Roman world: the contribution of non-medical sources. Arch Environ Occup H, 66(1):54-5. doi: 10.1080/19338244.2011.538656

Rodríguez-Villamizar, L.A., Jaimes, D.C., Manquián-Tejos, A., Sánchez L.H.2015. Human mercury exposure and irregular menstrual cycles in relation to artisanal gold mining in Colombia. Biomedica. 35:38–45.

Roulet, M; Lucotte, M; Canuel, R; Rheault, I; Tran, S; Gog, YGD; Farella, N; Do Vale, RS; Passos, CJS; da Silva, ED; Mergler, D; Amorim, M.1998.Distribution and partition of total mercury in waters of the Tapajos River Basin, Brazilian Amazon. Science of the Total Environment, 213(1–3):203–211.

Rowens, B., Guerrero-Betancourt, D., Gottlieb, C.A., Boyes, R.J., Eichenhorn, M.S.1991.Respiratory failure and death following acute inhalation of mercury vapor. A clinical and histologic perspective. Chest, 99(1): 185–190. doi: 10.1378/chest.99.1.185.

Sakamoto, M., Tatsuta, N.,Izumo, K., Phan, P., Vu. L.D., Yamamoto, M., Nakamura, M., Nakai, K., Murata, K. 2018. Health Impacts and Biomarkers of Prenatal Exposure to Methylmercury: Lessons from Minamata, Japan. Toxics. 6(3):45. doi: 10.3390/toxics6030045

Saldana, M., Collins, C.E., Gale, R., Backhouse, O. 2006. Diet-related mercury poisoning resulting in visual loss. Br J Ophthalmol. 90(11):1432-4. doi: 10.1136/bjo.2006.094821.

Smiechowicz, J.,Skoczynska, A., Nieckula-Szwarc, A., Kulpa, K.,Kübler, A. 2017.Occupational mercury vapour poisoning with a respiratory failure, pneumomediastinum and severe quadriparesis. SAGE Open Med Case Rep, 5:2050313X17695472. doi: 10.1177/2050313X17695472.

Solan, T.D.,Lindow, S.W. 2014. Mercury exposure in pregnancy: a review. J Perinatal Med. 42(6):725-9. doi: 10.1515/jpm-2013-0349

Song, Y., Lee, C.K., Kim, K.H., Lee, J.T., Suh, C., Kim, S.Y., Kim, J.H., Son, B.C., Kim, D.H., and Lee, S. 2016. Factors associated with total mercury concentrations in maternal blood, cord blood, and breast milk among pregnant women in Busan, Korea. Asia. Pac. J. Clin. Nutr, 25: 340–349.

Stacchiotti, A., Morandini, F.,Bettoni, F., Schena, I.,Lavazza, A., Grigolato, P.G., Apostoli, P., Rezzani, R., and Aleo, M.F. 2009. Stress proteins and oxidative damage in a renal derived cell line exposed to inorganic mercury and lead. Toxicology, 264: 215–224.

Study Group . MinamataDisease. Kumamoto University; Kumamoto, Japan: 1966.

Sukhn, C., Awwad, J., Ghantous, A., Zaatari, G. 2018. Associations of semen quality with non-essential heavy metals in blood and seminal fluid: data from the environment and male infertility (EMI) study in lebanon. J Assist Reprod Genet, 35: 1691- 1701.

Szász, A., Barna, B., Gajda, Z., Galbác, G., Kirsch-Volders, M., Szente, M. 2002. Effects of continuous low-dose exposure to organic and inorganic mercury during development on epileptogenicity in rats. Neurotoxicology, 23(2):197-206. doi: 10.1016/s0161-813x(02)00022-0.

Takeuchi, T., Eto, K. 1999. The Pathology of MinamataDisease. Kyushu University Press; Fukuoka, Japan:

Teixeira, F.B, de Oliveira, A.C.A,.Leão, L.K.R., Fagundes, N.C.F., Fernandes, R.M., Fernandes, L.M.P., da Silva, M.C.F., Amado, L.L., Sagica, F.E.S., de Oliveira, E.H.C., Crespo-Lopez, M.E., Maia, C.S.F., Lima, R.R. 2018. Exposure to Inorganic Mercury Causes

Oxidative Stress, Cell Death, and Functional Deficits in the Motor Cortex. Front MolNeurosci,11:125. doi: 10.3389/fnmol.2018.00125.
Tokuomi, H., Okajima, T., Kanai, J., Tsunoda, M., Ichiyasu, Y., Misumi, H., Shimomura, K., Takaba, M. 1961. Minamata disease. World Neurol. 2:536–545.
Trebucobich, M. S., Hazelhoff M. H., Chevalier A. A., Passamonti S., Brandoni A. M., Torres A. M. 2014. Protein expression of kidney and liver bilitranslocase in rats exposed to mercuric chloride–a potential tissular biomarker of toxicity. ToxicolLett, 225(2): 305–310. doi:10.1016/j.toxlet.2013.11.022
Ung CY., Lam SH., Hlaing MM., Winata CL., Korzh S.,Mathavan S, Gong, Zhiyuan.2010. Mercury-induced hepatotoxicity in zebrafish: in vivo mechanistic insights from transcriptome analysis, phenotype anchoring and targeted gene expression validation. BMC Genomics,11:212. doi: 10.1186/1471-2164-11-212
UNIDO (United Nations Industrial Development Organization) Protocols for Environmental and Health Assessment of Mercury Released by Artisanal and Small-Scale Gold Miners. United Nations Industrial Development Organization; Vienna, Austria: 2008.
Vassallo, D.V., Moreira, C.M., Oliveira, E.M.,Bertollo, D.M.,Veloso, T.C. 1999. Effects of mercury on the isolated heart muscle are prevented by DTT and cysteine. Toxicology and Applied Pharmacology, 156(2):113–118.
Wadaan, M.A. 2009. Effects of mercury exposure on blood chemistry and liver histopathology of male rats. J PharmacolToxicol, 4(3):126–131.
Wakita, Y. 1987. Hypertension induced by methyl mercury in rats. Toxicology and Applied Pharmacology, 89(1):144–147.
Yawei, C., Jing, S., Wenju, S., Yupeng, L., Ping, Z.,Liping, H. 2021. Mercury as a cause of membranous nephropathy and Guillain–Barre syndrome: case report and literature review. Journal of International Medical Research,49(3):300060521999756. doi: 10.1177/0300060521999756
Yin, Z., Lee, E., Ni, M., Jiang, H.,Milatovic, D.,Rongzhu, L., Farina, M., Rocha, J.B.,Aschner. 2011. Methylmercury-induced alterations in astrocyte functions are attenuated by ebselen. NeuroToxicology, 32(3):291–299.
Zalups, R.K., and Koropatnick, J. 2000. Temporal changes in metallothionein gene transcription in rat kidney and liver: relationship to content of mercury and metallothionein protein. J. Pharmacol. Exp. Ther, 295(1):74-82.
Zalups, R.K., Joshee, L., and Bridges, C.C. 2014. Novel Hg^{2+}-induced nephropathy in rats and mice lacking mrp2: Evidence of axial heterogeneity in the handling of Hg^{2+} along the proximal tubule. Toxicol. Sci, 142 (1): 250–260. doi: 10.1093/toxsci/kfu171
Zhenzhen,Gao., Na, Wu., Xuqin, Du., Huiling, Li.,Xue, Mei., Yuguo, Song. 2022. Toxic Nephropathy Secondary to Chronic Mercury Poisoning: Clinical Characteristics and Outcomes, Kidney International Reports, 7 (6): 1189-1197.