

International Journal of Immunology Research



ISSN Print: 2664-8865
ISSN Online: 2664-8873
Impact Factor: RJIF 5.48
IJIR 2024; 6(1): 01-03
www.immunologyjournal.in
Received: 02-11-2023
Accepted: 03-12-2023

Piusha Mondal
Department of Microbiology,
School of Life Sciences, Swami
Vivekananda University,
Barrackpore, West Bengal,
India

Priyankar Pal
Department of Biotechnology,
School of Life Sciences, Swami
Vivekananda University,
Barrackpore, West Bengal,
India

Immunotoxicity caused by excessive mercury exposure: A brief overview

Piusha Mondal and Priyankar Pal

DOI: <https://doi.org/10.33545/26648865.2024.v6.i1.a.21>

Abstract

Mercury (Hg) is a widely dispersed environmental and industrial xenobiotic. The threat of mercury exposure to human populations is alarming and can arise through an array of pathways, including occupational, food contamination, excessive use of medicinal or cosmetic treatments, and fossil fuel emissions. The chemical forms of Hg include inorganic mercury (iHg), organic mercury (oHg), and elemental mercury (Hg⁰). Among them, oHg is most frequently found as (mono) methyl mercury (MeHg) and ethyl mercury (EtHg). Cytotoxicity of mercury in its divalent ionic form, Hg⁺², has been related to cellular oxidative stress, and reaction of Hg⁺² with thiols results in the creation of mercaptans, which deplete the thiol-based antioxidant buffers made up primarily of glutathione in cells. The literature has consistently noted elevated GSSG/GSH ratio and H₂O₂ generation in various cell exposed to mercury-containing chemicals. It has been known that mercury indemnities the immune system function, most likely due to its damaging effects on polymorphonuclear leukocytes (PMNs). Mercury is also thought to suppress the production of adrenocorticosteroids, which prevents the normal stimulation of PMNs and also has an impact on PMN function by impairing their capacity to destroy the foreign substances. Mercury can affect immune cell activity and formation, as well as regulate the synthesis of interferon-gamma and interleukin-2 in the central nervous system. Hg has been demonstrated to increase explosion and cytokine synthesis from the T lymphocytes. Mercuric chloride (HgCl₂) endorses the release of histamine as well as cytokines, such as IL-4 and tumour necrosis factor-alpha (TNF-α), from mast cells. Additionally, HgCl₂ increases the secretion of the histamine from a rat basophil cell line and immunoglobulin E-mediated arbitrator release from the human basophils. Several immune or autoimmune diseases, such as autism/attention deficit hyperactivity disorder, allergic disease, eczema, arthritis, amyotrophic lateral sclerosis, autoimmune thyroiditis, epilepsy, rheumatoid arthritis, psoriasis, multiple sclerosis, scleroderma, schizophrenia, and systemic lupus erythematosus, are linked to mercury toxicity. The review research has focused on the mechanistic theory of immunological damage caused by mercury.

Keywords: Mercury, lymphocytes, immune-globulins, inflammatory cytokines, auto-immune disorders

Introduction

Periodically Table-wise Mercury (Hg), a d-block element that is visible in liquid media, is naturally occurring on rocks, the earth's crust, and soils. It is also widely distributed in complex compounds found in the shells of many sea creatures. However, long-term exposure to the mercury or its compounds can cause toxicity in humans (Baker 2008) ^[1]. Mercury is a neurotoxic element that tethers the mast cell to cause immunotoxicity and increases allergic reactions. It causes nervous system damage and modifies the enzymatic and genetic systems (Puri and Roche 2008) ^[12]. Tremors, sleeplessness, memory loss, neuromuscular effects, excruciating headaches, motor dysfunction, etc. are some of the common symptoms that patients may experience (D'Souza, Fombonne, and Ward 2006) ^[2]. There are various methods of introducing Mercury into the human body, these are –

1. Eating excessive amounts of seafood that contains high levels of methylmercury, the toxic form of mercury that has harmful effects on the body, is a common way to absorb mercury.
2. Inhaling mercury vapour while conducting industrial processes is an uncommon method.

Corresponding Author:
Priyankar Pal
Department of Biotechnology,
School of Life Sciences, Swami
Vivekananda University,
Barrackpore, West Bengal,
India

Mercury comes in two varieties: inorganic mercury and organic mercury

Excessive exposure to inorganic mercury can harm the kidney, nervous system, gastrointestinal tract, and other organ systems while the gastrointestinal tract absorbs the mercury. When mercury and carbon mix, organic mercury compounds are created (Monroe and Halvorsen 2009) [10]. If the toxicity is not treated, it can also be inhaled and cause harm to the central nervous system, which includes the brain and spine. The most hazardous aspect is that we are ignorant of or lack sufficient understanding of this delicate subject.

The detrimental effects of mercury and its related compounds on human bodies will be the main topic of this review article. It will also discuss how these compounds cause issues with the immune system, nervous system, enzymatic and genetic complexes, and other organ systems (Kirshenbaum *et al.* 2003) [9].

Mechanism of mercury induced immune-toxicity

The body experiences mercury-mediated immunotoxicity when normal, healthy cells begin to accumulate mercury. The following are some typical methods or mechanisms of this phenomenon.

1. Passive diffusion

Mercury vapour is thought to pass through cell membranes by passive diffusion, however some research has also suggested that protein transport of small, uncharged molecules may also play a role in this transport.

2. Inorganic Mercury

Some compounds known as metallic mercury (Hg), mercury ions (Hg¹), or mercury ions (Hg²) are known to cause inorganic mercury toxicity in humans. These compounds are primarily found in forms of mercury salts, such as batteries. It makes its entry point into the body through the skin or mouth, where it is absorbed at a rate of up to 10% by the digestive system. It is an extremely hazardous substance (Strenzke *et al.* 2001) [15]. For its low lipid solubility, which causes it to accumulate primarily in the kidney and cause significant renal damage, it is able to restrict CNS penetration. Additionally, its slow elimination and prolonged acquaintance allow for noteworthy CNS accretion of mercuric ions, which can lead to toxicity. Extended skin exposure to the inorganic mercury can also result in elevated body toxicity. Mercury's hazardous forms and insufficient renal excretion are thought to contribute to long-term exposure and accumulation in the brain and spinal cord (Schedle *et al.* 1998) [13].

3. Organic Mercury

There are three types of inorganic mercury that can be toxic to humans: aryl, short- and long-chain alkyl compounds. Because organic mercury has inherent qualities like mild corrosiveness and lipid solubility, it is more thoroughly absorbed from the GI tract than inorganic salts. After being absorbed by gastrointestinal tract, organic mercury is transformed into inorganic forms by aryl and long chain alkyl compounds, which have a toxicity comparable to that of inorganic forms. Because of their high solubility in lipids, short chain alkyl compounds are absorbed 90–95% by the GI tract and stay stable in their original forms. They are distributed evenly throughout the body and accumulate in the kidney, liver, brain, hair, and skin. Additionally, they penetrate the placenta, the blood-brain barrier, and erythrocytes, resulting in teratogen effects, elevated blood-to-plasma ratios, and neurologic symptoms, respectively.

Effects of the mercury toxicity

Mercury-mediated toxicity can have moderate to extremely important effects on healthy, normal cells. It may impact the breakdown of the neurological system, dermal intestine, or kidneys. These effects are addressed in more detail below:

1. Renal effects: One common direct renal toxic effect is necrosis of the proximal tubules; therefore, if renal abnormalities go unexplained and neuropsychiatric disturbances occur, the doctor should think about mercury toxicity (Young, Geier, and Geier 2008) [17]. Thermometers, barometers, batteries, dental amalgams, bronzing, and other items are among the sources of elemental mercury toxicity.

2. Effects on Nervous System: Methyl mercury causes mental disorders, visual loss, ataxia, hearing loss, and neuropathy, which are among its most severe effects on central nervous system. The patients who were exposed in utero suffered the most severe neurologic damages in the form of diffusion and widespread neuronal atrophy. Ninety percent of alkyl mercury excretion takes the form of faeces (Duraisamy Kempuraj *et al.* 2005) [8]. Mercury damages nervous system in a number of ways, including binding to sulphides groups and impeding important enzymes that are involved in protein repair, oxidative damage prevention, and the cellular stress response (Paus, Theoharides, and Arck 2006) [11].

The muscarinic cholinergic system in the brain stem and occipital cortices is disrupted by methylmercury. Additionally, inactive sodium-potassium adenosine triphosphatase causes membrane depolarization and calcium entry, which ultimately leads to cell death. These effects may be simultaneously triggered and ultimately culminate in apoptosis (D. Kempuraj *et al.* 2008) [6]. Excessive excitotoxins and nitric oxide system dysregulation in rodents exposed to methylmercury have been found to cause sulcal artery compression and subsequent ischemia, which can lead to calcium and parietal cell loss as well as gliosis. Selenium is used as an enzymatic cofactor in several cellular biochemical pathways, but methylmercury may sequester element selenium and disrupt these pathways.

Neurotoxicity can be developed CNS by -

1. Inhibition of macromolecules synthesis (DNA, RNA and proteins)
2. Microtubules disruption
3. Increase in intracellular calcium with disturbance of neurotransmitter function

Discussions

This is the initial report that we are aware of that demonstrates how human cultured mast cells can secrete VEGF and IL-6 when exposed to inorganic mercury at concentrations as little as 0.1 mM. According to one study, primary lung as well as human leukemic muscle cells can release histamine when exposed to HgCl₂. Mercury has been demonstrated to trigger the release of beta hexosaminidase, IL-4, and TNF alpha from cultured mast cells derived from mouse bone marrow (Duraisamy Kempuraj *et al.* 2004) [7]. Only at the concentrations of 1 and 10 mM does HgCl₂ improve allergic release from the human basophils; it has no effect on histamine and IL-4 release on its own. This also applies to the release of IL-4 from the rat mast cells. At blood levels of 1 mM, clinical symptoms of the mercury poisoning may be anticipated. Lower mercury concentrations in the subpopulation of susceptible patients may cause brain mast cells to respond. It is unclear exactly how heavy metal neurotoxicity works. In PC 12 cells, mercury raises cytosolic calcium levels, and in thymus

lymphocytes, thimerosal does the same (Dastyk *et al.* 1999) [3]. The chief dietary source of the neurotoxic mercury compounds is the ingestion of the methylmercury from fish, which was previously related to the neurological damage (Suzuki *et al.* 2001) [16]. ASD are group of pervasive developmental disorders that includes autistic disorders also known as PDF-NOS (Jiang and Möller 1995) [5]. They are distinguished by varying degrees of attention, cognitive learning, sensory abnormalities, repetitive and stereotypical behaviour, and dysfunctional social and communication skills. Nevertheless, no specific pathogenesis is known, no biomarkers exist, and no proven treatment exists. Epigenetic acquaintance to the environmental factors combined with genetic or biochemical susceptibility may result in ASD (Geier *et al.* 2008) [17]. It leads to neuroimmune disorders relating mast cell activation (Stehr-Green *et al.* 2003) [14].

Conclusion

The current study's findings provide biological credence to the theory that the mercury may be a contributing factor to immunotoxicity, harming not only the nervous system but also other organs in the human body, including the pathogenesis of ASD. This is because mercury can induce mast cell release of VEGF and IL-6, which can disrupt the blood-brain barrier and allow inflammation of the brain. The possessions of mercury and thimerosal, either by themselves or in combination with immunological and allergic triggers, should be further studied.

Future thought

Although we have researched these conditions and their malfunctions in an effort to treat the heavy metal neurotoxicity, we still need to learn enough to effectively manage these kinds of toxicities. Additional research may support these ideas.

Acknowledgement

I am happy that I have the chance to work on this review of a significant subject thanks to the esteemed teachers of Swami Vivekananda University. And I am appreciative of all the authors and researchers who have worked on this subject.

Reference

1. Baker JP. Mercury, Vaccines, and Autism: One Controversy, Three Histories. *American Journal of Public Health*, 2008, 98(2).
2. D'Souza Y, Fombonne E, Ward BJ. No Evidence of Persisting Measles Virus in Peripheral Blood Mononuclear Cells from Children with Autism Spectrum Disorder. *Pediatrics*, 2006, 118(4).
3. Dastyk J, Walczak-Drzewiecka A, Wyczolkowska J, Metcalfe DD. Murine Mast Cells Exposed to Mercuric Chloride Release Granule-Associated N-Acetyl- β -D-Hexosaminidase and Secrete IL4 and TNF- α . *Journal of Allergy and Clinical Immunology*, 1999, 103(6).
4. Geier DA, King PG, Sykes LK, Geier MR. A Comprehensive Review of Mercury Provoked Autism. *Indian Journal of Medical Research*. 2008, 128(4).
5. Jiang Y, Möller G. *In vitro* Effects of HgCl₂ on Murine Lymphocytes. I. Preferable Activation of CD4⁺ T Cells in a Responder Strain. *The Journal of Immunology*, 1995, 154(7).
6. Kempuraj D. Luteolin Inhibits Myelin Basic Protein-Induced Human Mast Cell Activation and Mast Cell-Dependent Stimulation of Jurkat T Cells. *British Journal of Pharmacology*, 2008, 155(7).
7. Kempuraj D. Corticotropin-Releasing Hormone and Its Structurally Related Urocortin Are Synthesized and Secreted by Human Mast Cells. *Endocrinology*, 2004, 145(1).
8. Kempuraj D, Madhappan B, Christodoulou S, Boucher W, Cao J, Papadopoulou N, *et al.* Flavonols Inhibit Proinflammatory Mediator Release, Intracellular Calcium Ion Levels and Protein Kinase C Theta Phosphorylation in Human Mast Cells. *British Journal of Pharmacology*, 2005, 145(7).
9. Kirshenbaum AS. Characterization of Novel Stem Cell Factor Responsive Human Mast Cell Lines LAD 1 and 2 Established from a Patient with Mast Cell Sarcoma/Leukemia; Activation Following Aggregation of Fc ϵ RI or Fc γ RI. *Leukemia Research*, 2003, 27(8).
10. Monroe RK, Halvorsen SW. Environmental Toxicants Inhibit Neuronal Jak Tyrosine Kinase by Mitochondrial Disruption. *Neuro Toxicology*, 2009, 30(4).
11. Paus R, Theoharides TC, Arck PC. Neuroimmunoendocrine Circuitry of the 'Brain-Skin Connection.' *Trends in Immunology*, 2006, 27(1).
12. Puri N, Roche PA. Mast Cells Possess Distinct Secretory Granule Subsets Whose Exocytosis Is Regulated by Different SNARE Isoforms. *Proceedings of the National Academy of Sciences of the United States of America*, 2008, 105(7).
13. Schedle A. Metal Ion-Induced Toxic Histamine Release from Human Basophils and Mast Cells. *Journal of Biomedical Materials Research*, 1998, 39(4).
14. Stehr-Green P. Autism and Thimerosal-Containing Vaccines: Lack of Consistent Evidence for an Association. *American Journal of Preventive Medicine*, 2003, 25(2).
15. Strenzke N. Mercuric Chloride Enhances Immunoglobulin E-Dependent Mediator Release from Human Basophils. *Toxicology and Applied Pharmacology*, 2001, 174(3).
16. Suzuki Y. Exposure of RBL-2H3 Mast Cells to Ag⁺ Induces Cell Degranulation and Mediator Release. *Biochemical and Biophysical Research Communications*, 2001, 283(3).
17. Young HA, Geier DA, Geier MR. Thimerosal Exposure in Infants and Neurodevelopmental Disorders: An Assessment of Computerized Medical Records in the Vaccine Safety Datalink. *Journal of the Neurological Sciences*, 2008, 271(1–2).

How to Cite This Article

Mondal P, Pal P. Immunotoxicity caused by excessive mercury exposure: A brief overview. *International Journal of Immunology Research*. 2024;6(1):01-03.

Creative Commons (CC) License

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International (CC BY-NC-SA 4.0) License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.