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| RESEARCH ARTICLE

Heavy Metals and Cardiovascular Disease on Wetlands

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| ABSTRACT
Heavy metals are metal elements with a relatively high density compared to water. One area that is vulnerable to heavy metal pollution is the wetland environment. In South Kalimantan, an alkaline land area, pollution is mainly caused by mining activities, especially coal mining and oil palm plantation activities. The presence of heavy metals in the sediments of the Martapura River in South Kalimantan, which have passed the threshold for sediment contamination, includes Mn, Fe and Hg. The potential link between chronic heavy metal exposure and cardiovascular disease (CVD) has several implications. Although the cardiovascular system is not usually viewed as the main target of heavy metal toxicity, imbalances in antioxidant protection mechanisms lead to oxidative stress in cells as a major effect of heavy metal exposure. Heavy metals can cause oxidative stress by producing reactive oxygen species (ROS). Heavy metals are associated with an increase in systemic inflammation. They can lead to impaired immune function and accumulation of immune complexes, causing CVD, including the uncontrolled release of inflammatory cytokines, kidney damage, and central nervous system stimulation. However, some research results are contradictory and say no relationship exists between heavy metals, such as mercury, and cardiovascular disease. The presence of heavy metals is still a health risk in wetlands. Metal content that crosses this threshold can be a cause or a risk factor for cardiovascular disease. The effects of heavy metal content, such as mercury, on health, especially cardiovascular disease, are still not fully understood, requiring further investigation and research.

| KEYWORDS

Heavy Metals, Cardiovascular Disease, Wetlands, Mercury, Oxidative Stress

| ARTICLE INFORMATION

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1. Introduction

Wetlands, as a translation of "*lahan basah*", was only known in Indonesia around 1990. Previously, Indonesian people called wetland areas based on each type's physical form/name, such as swamps, lakes, rice fields, ponds, and so on. In addition, various sectoral departments also define wetlands based on the sector of their respective work areas. The physical definition of wetlands, which is used to equate the perceptions of all parties, has become standardized since the ratification of the 1991 Ramsar Convention, namely: "Swamp, brackish, peatland and water areas; permanent or temporary; with stagnant or flowing water; unsalted, brackish, or salty; including areas of sea waters whose depth is not more than six meters at low tide (Harahap, 2016).

Pollution is currently happening everywhere; the water crisis is also happening everywhere; in general, the water crisis is caused by pollution from industrial, household or agricultural wastewater. In addition to the decline in water quality due to pollution, the water crisis also occurs due to reduced water availability and erosion due to upstream forest clearing and changes in land use upstream and downstream. The shrinking of the water supply in several major rivers in Kalimantan is a terrible phenomenon; these rivers are experiencing siltation due to a lack of water during the dry season and increased erosion and sedimentation (Pahruddin, 2017).

In South Kalimantan, the water crisis is mainly caused by mining activities, especially coal mining and by oil palm plantation activities, both of which are very intensively cultivated in the province of South Kalimantan. Mining activities cause water quality contamination from a chemical point of view, namely metals because mining activities dismantle rock layers in the soil containing heavy metals. Metals can be classified into two types: heavy and light metals. Heavy metals are metals weighing more than 5 g/cm3. Heavy metals are referred to as non-essential metals and, at certain levels, can be toxic to living things. Heavy metals are natural components in soil. These components cannot be degraded (non-degradable) or destroyed. These compounds can enter the body through food, drinking water, and air. Heavy metals harmful to humans include lead, copper, mercury, cadmium, and chromium (Irianti, 2017). This article will discuss more about heavy metals and cardiovascular disease in wetlands.

2. Wetlands and Heavy Metals in Borneo South

South Kalimantan is one of the provinces rich in natural resources in the form of minerals, coal, oil, gold and various natural products. Regarding topography, South Kalimantan consists of 4 (four) soil types, namely alluvial, hilly swamp plains and mountains, with dominant soil types, namely red-yellow podzolic and alluvial. Wetlands have an important role in environmental preservation, including contributing to biodiversity, climate balancing, and being a source of water circulation and food for the local community. Communities use wetlands to meet various needs, especially the necessities of life. The Banjar people in South Kalimantan use the wetlands for farming, raising fish and cultivating crops. However, using these wetlands is also a cause of damage and loss of wetlands (Lestari, 2019).

Dwiyatno's research results in 2008 showed that the content of heavy metals (Hg, Pb, Cd, and Cu) in fish in the waters estuary of S. Barito is still below the permissible threshold, so it is safe for consumption. However, attention should be paid to the level of consumption of haruan fish because the metal content of Hg is relatively high. Other research in the waters of South Kalimantan only shows code Pb (Lead), which is still below the maximum for heavy metal contamination. However, this study did not examine the content of other metals (Panghiyangani, 2019).

In a 2020 study on the Martapura River, South Kalimantan, the heavy metal Mn content obtained ranged from 494-2,142 ppm with an average of 248.77 ppm. Compared with the threshold for Mn metal in sediments, all sampling locations have been polluted by Mn metal. The high value of Mn can be caused by residual coal mining activities, in which toxic materials left behind from coal mining and processing contain heavy metals, one of which is Mn. Besides mining, Mn can also be produced from the weathering of rocks in water basins or volcanic activity, derived from active substances where used battery stones are thrown into rivers and coasts. The content of heavy metal Fe in the Martapura River sediment samples ranged from 48,000-68,800 ppm with an average of 60,133.33 ppm. Compared with the threshold, Fe metal in all sampling locations has exceeded the sediment contamination threshold, namely 68800 ppm. The content of heavy metal Fe in sediments elsewhere, such as in the Ombilin River, shows values ranging from 71,840-111,900 ppm with an average of 96,181 ppm which has exceeded the sediment contamination threshold, while in the Citarum River, it ranges from 44,900-56,000 ppm indicating that it is still below the threshold. Sediment contamination. The high content of Fe in river sediments can be caused by weathering of bedrock in this area, which is known that the Martapura River originates in the Bobaris Mountains, where one of the bedrock is an ultramafic igneous rock (Adhani, 2017).

A gold mine in Mataraman District, Banjar Regency, South Kalimantan, is also thought to have caused the high Hg content in the Martapura River, where the river flow from that area enters the Martapura River (Adhani, 2017).

The presence of heavy metals in the sediments of the Martapura River in South Kalimantan, which have passed the threshold for sediment contamination, includes Mn, Fe and Hg. The high content of these three heavy metals is thought to originate from the weathering process of bedrock. It is also suspected to be caused by the remnants of coal and gold mining processes and also the use of pesticides around the study area (Adhani, 2017).

Table 1. Heavy Metal Content in Martapura River Sediments[6]

	Heavy Metal Concentration (ppm)				
Sample	**Cu**	**Zn**	**Mn**	**Fe**	**Hg**
1	69	113	921	61.100	5.775
2	51	93	1.299	58.600	0.108
3	40	79	1.026	48.000	0.092
4	75	106	2.142	68.800	0.115
5	82	103	1.786	63.100	0.115
6	68	147	815	58.600	0.205
7	72	131	991	64.800	0.154
8	67	161	797	67.300	0.169

9	43	110	494	50.900	0.123
Average	63	115,88	1.141,22	60.133,33	0.761
Minimum Value	40	79	494	48.000	0.092
Maximum Value	82	161	2.142	68.800	5.775
Threshold	108	271	248.77	20	0.02-0.35

3. The Effects of Heavy Metals on Health

Heavy metals are natural components in soil. This component cannot be degraded (non-degradable) or destroyed. These compounds can enter the body through food, drinking water, and air. At low levels, heavy metals are needed by living things to regulate various chemical and physiological functions of the body. This is commonly known in terms of trace elements, namely chemical elements needed by living organisms in very small quantities (less than 0.1% of the volume). As a trace element, some heavy metals such as copper (Cu), selenium (Se), iron (Fe) and zinc (Zn) are very important for the body. Heavy metals can be harmful or toxic when present in excessive levels in the body (Mu'jijah, 2019).

Only those toxic to living things are classified as heavy metals. Heavy metals include essential Zn, Cu, and Se and non-essential ones, such as Hg, Pb, Cd, and As. Cases of heavy metal poisoning often result from environmental pollution by heavy metals themselves, such as using metals as pesticides and fertilizers or due to the disposal of factory waste that uses metals. Essential metals such as Cu and Zn are needed as animal nutritional elements at certain levels. However, the uses of non-essential metals such as Hg, Pb, Cd, and as are currently unknown. When heavy metals enter the human body, they accumulate in the body's tissues and cannot be excreted outside the body. At levels that are already high in the human body, it will cause serious negative effects (Mu'jijah et al., 2019).

Meanwhile, the microelement group is a group of heavy metals with no function for the body. Examples are lead (Pb), mercury (Hg), arsenic (As) and cadmium (Cd). These compounds are even very dangerous and toxic to humans. Heavy metals are non-degradable and easily absorbed (Irianti, *2017)*.

Heavy metals can also cause harm to aquatic organisms. Sources of metal pollution mostly come from mining, metal smelting, and other industries. They can also come from domestic waste that uses metals and agricultural land that uses metal-containing fertilizers. Pollutant retention depends on its biological half-life. Thus, a pollutant must exhibit relatively high resistance to destruction or disposal by living organisms to allow sufficient uptake time to achieve high concentrations. The content of heavy metals will increase over time. For example, plants in that habitat are the first organisms to be affected by a heavy metal content in the soil. If humans consume these plants, heavy metals can collect in the body and remain for a long time as accumulated poisons, commonly known as bioaccumulation. This process can occur by direct absorption from the environment or through foodstuffs. Pollutants in living things through food can arise from the same source. So in a natural food chain, pollution can be moved from one level to another (Lestari et al., 2019)

Bioaccumulation is an increase in the concentration of a chemical substance in the body creature that lives for a long time, compared to levels of chemical substances in nature. Excessive levels because heavy metals cannot be metabolized and cannot undergo biotransformation to other compounds. Heavy metals can only be excreted by the body through the kidneys in the form of ions, and these ions can cause impaired kidney function.

Besides being naturally occurring, the causes of heavy metal content in soil include agrochemical materials such as fertilizers and pesticides, contamination from motor vehicle exhaust, fuel oil, household waste, industrial waste, and mining. The soil's heavy metals content is influenced by environmental factors such as soil acidity, organic matter, temperature, texture, clay minerals, and other elements. The degree of acidity (pH) is important in the metal transformation process. At low pH, the availability of some heavy metals can increase (Rizkiana et al., 2017)

The knowledge gained about heavy metal homeostasis has been growing rapidly for more than a decade. Although heavy metals have no known metabolic function, when present in the body, they interfere with normal cell processes, poisoning several organs. Heavy metals have absorption, which is bad, but once absorbed, it is slowly excreted and accumulates in the body, causing organ damage. Thus, their toxicity is largely due to their accumulation in biological tissues, including food animals such as fish, beef, and humans. The distribution of heavy metals in the body depends on their binding to circulating carrier molecules.
Its major impact on human health is primarily through occupational exposure, environmental pollution, and the accumulation of food, especially in vegetables grown in contaminated soil. Arsenic, cadmium, mercury and lead are the most likely causes of the

heavy metal-related illnesses observed in primary care medicine. Other exposures often accompany exposure to one heavy metal contaminant. Therefore, combined interactions may occur in populations exposed to metal alloys (Rizkiana et al., 2017).

Heavy metals are toxic because they may have a cumulative deleterious effect that can lead to chronic degenerative changes, particularly in the nervous system, liver and kidneys, and, in some cases, teratogenic and carcinogenic effects. The mechanism of toxicity of some heavy metals is still unknown, although enzymatic inhibition, disturbance of antioxidant metabolism and oxidative stress may play a role. Heavy metals produce many adverse health effects by forming free radicals, resulting in DNA damage, lipid peroxidation and depletion of sulfhydryl proteins (Baloch et al., 2020)

Heavy metals as environmental pollutants and promoters of oxidative stress are associated with many adverse effects on human health. There is growing concern about the physiological and behavioural effects of environmental heavy metals on the human population. Heavy metal poisoning in humans has acute and chronic effects on health and the environment. Although heavy metal toxicity at high levels of exposure is well known, a major concern today is the possibility that continued exposure to heavy metals at relatively low levels may cause adverse health effects. However, its contribution to CVD is still not fully understood. Recent studies show that the effect vascular of heavy metals can contribute to various pathological conditions, including diabetes mellitus and hypertension. However, the mechanism of action of heavy metal exposure is still unclear (Nair, 2018).

4. Heavy Metals and Cardiovascular Disease

The potential link between chronic heavy metal exposure and cardiovascular disease (CVD) has several implications. Although the cardiovascular system is not usually viewed as a primary target of heavy metal toxicity, review articles covering their role as cardiovascular toxicants are few, and the main concern of most reviews has been focused on imbalances in antioxidant protection mechanisms causing oxidative stress in cells as a major effect of their environmental exposure. Gene expression is altered by environmental influences, especially food components gene regulation, which can be affected by metal toxicity (Jaishankar et al., 2014).

Patients differ in the time of onset and risk factor dynamics, reflecting the complex pathophysiology of CVD. In contrast, genetically determined susceptibility to the environment, risk factors, system interactions cardiovascular with other organs such as the immune system, and the interaction between these risk factors in a person is a possible cause for the difference. Despite an increasing understanding of the genes, proteins, signalling pathways, cell-cell interactions, and systemic processes involved in CVD (initiation, development, and outcome), the relevance of environmental factors has yet to be discussed (Sevim, 2020).

Table 2. Risk Factors for Cardiovascular Disease[1]

Category	Example
Unmodifiable Risk Factors	1. Age 2. Male 3. Family History
Metabolic Risk Factors	1. Hypertension 2. Diabetes Mellitus / Glucose Intolerance 3. Metabolic Syndrome 4. Hyperlipidemia 5. Obesities/Overweight
Lifestyle Risk Factors	1. Smoke 2. Physical Activity 3. Food
New Risk Factor	1. Lipoprotein 2. Homocysteine 3. Inflammatory markers (example: C-Reactive Protein) 4. Prothrombotic factors (example: Fibrinogen 5. Micro-elements (example: Selenium, Zinc, Copper) 6. Heavy Metals (example: arsenic, lead, mercury)

Heavy metals (As, Cd, Hg and Pb) can cause oxidative stress by producing reactive oxygen species (ROS), including superoxide radicals, hydrogen peroxide and nitric oxide. Many metals have been shown to enhance lipid peroxidation or free radical-driven oxidative modification of low-density lipoprotein (ox-LDL), a well-recognized causal event early in the development of atherosclerosis. Cd can damage vascular tissue, cause endothelial dysfunction, and increase atherosclerosis through oxidative mechanisms (Genchi et al. 2017).

Heavy metals are associated with an increase in systemic inflammation, where essential metal deficiencies and excess toxic metals can lead to impaired immune function and accumulation of immune complexes, and through a series of interrelated processes, cause CVD, including the uncontrolled release of inflammatory cytokines, kidney damage, and stimulation central nerve system. Metals increase oxidative stress and inflammation leading to the formation of atherosclerotic lesions as it has been associated with increased intravascular inflammation by upregulating interleukin 6 (IL-6), tumor necrosis factor-a (TNF-a), monocyte chemotactic protein, vascular cell adhesion molecule 1 (VCAM-1), and intercellular adhesion molecule (ICCAM). Cd has also been associated with inflammatory and coagulation disorders, including increased blood levels of C-reactive protein (CRP) and fibrinogen in the US general population and VCAM-1 in animal studies. Both oxidative stress and increased systemic inflammation caused by exposure to toxic metals contribute to the development of atherosclerosis (2020).

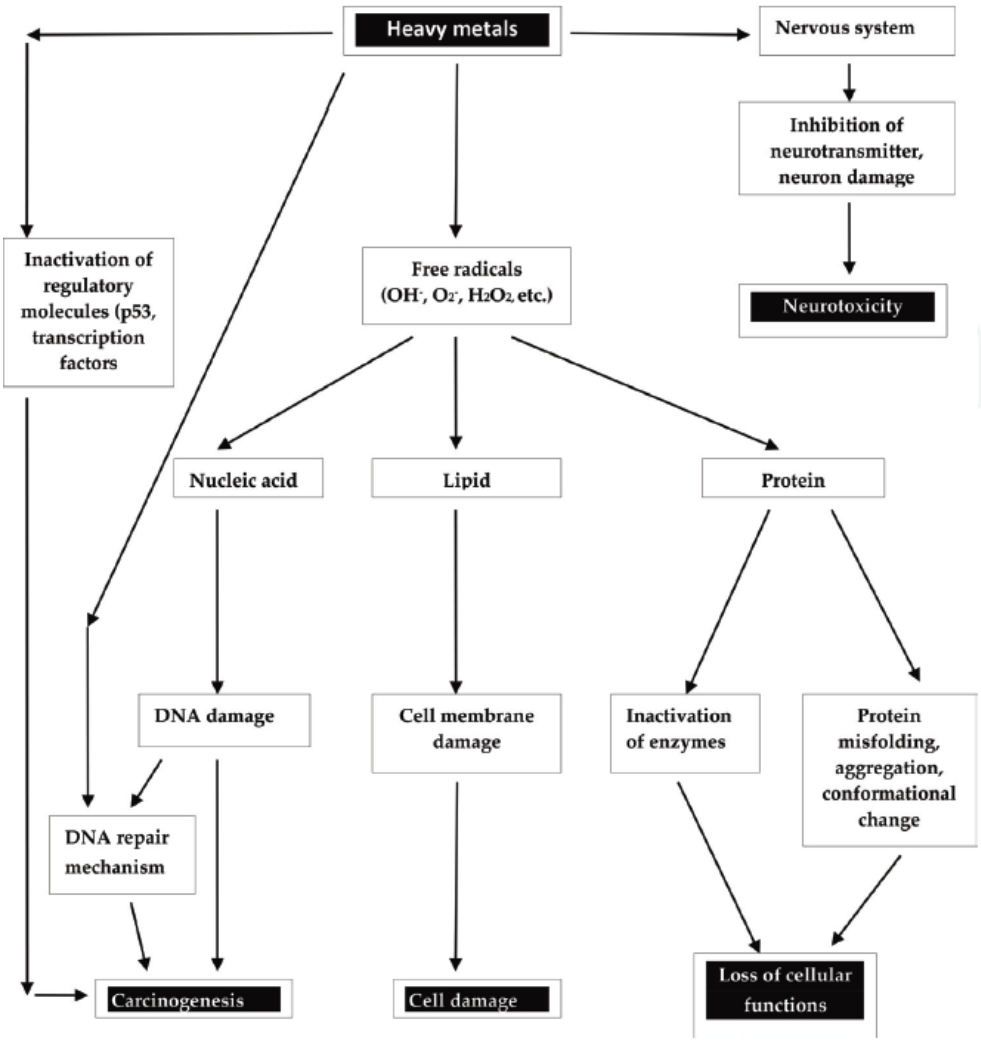


Figure 1. Pathway of heavy metals sources and exposure to humans[17]

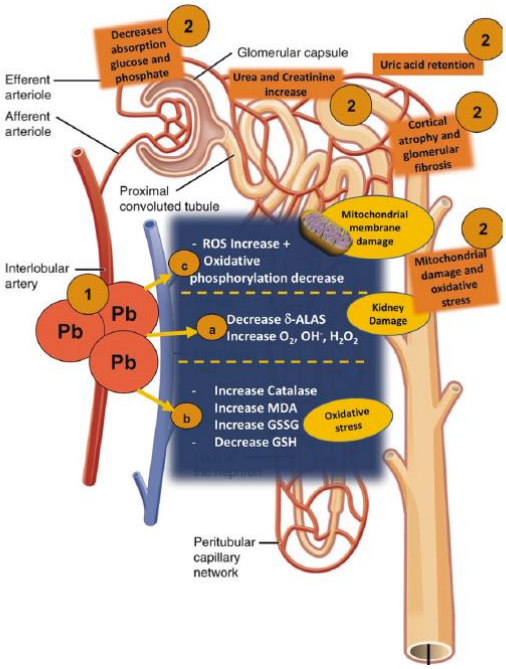


Figure 2. Mechanism of Pb Toxicity[18]

Pb is known to induce ROS production, and Pb-induced oxidative stress can cause the degradation of proteins, nucleic acids, and lipid peroxidation. Cu, along with Zn, is essential for a balanced oxidant-antioxidant mechanism, and an imbalance of Cu and Zn may increase the susceptibility to toxic metal-induced oxidative damage in b-cells and contribute to the pathogenesis of insulin resistance. Cr is a component or activator of several enzymes, most of which are antioxidants. She is a cofactor of antioxidant enzymes that enables glutathione peroxidase to reduce Cd/Pb-induced oxidative stress (Genchi, 2017).

Heavy metals are associated with an increase in systemic inflammation, in which essential metal deficiencies and excess toxic metals can lead to impaired immune function and accumulation of immune complexes, and through a series of interrelated processes, lead to CVD, including the uncontrolled release of inflammatory cytokines, kidney damage, and systemic stimulation central nervousness. Metals increase oxidative stress and inflammation leading to the formation of atherosclerotic lesions as it has been associated with increased intravascular inflammation by upregulating interleukin 6 (IL-6), tumor necrosis factor-a (TNF-a), monocyte chemotactic protein, vascular cell adhesion molecule 1 (VCAM-1), and intercellular adhesion molecule (ICCAM). Cd has also been associated with inflammatory and coagulation disorders, including increased blood levels of C-reactive protein (CRP) and fibrinogen in the US general population and VCAM-1. Both oxidative stress and increased systemic inflammation induced by toxic metal exposure contribute to the development of atherosclerosis (Sudarningsih, 2021).

Heavy metals compete with essential metals for various physiological functions influencing CVD risk. Heavy metals compete with essential metals for absorption and excretion; metal transport in the body, i.e. binding target proteins; and metabolism and sequestration of toxic metals. Part of Pb's toxicity stems from its ability to mimic other essential metals, for example, Ca, Fe, and Zn, because it binds to and interacts with many of the same enzymes as these essential metals, thereby interfering with the ability of the enzymes to catalyze normal reactions. Cd and Pb have chemical and physical properties similar to Zn and compete for the binding sites of enzymatic and metal absorption proteins. Therefore, if Zn deficiency occurs and exposure to this toxic metal increases, the body will use Cd and Pb as a substitute for Zn. Cd also competes with Fe for access to intestinal metal uptake transporters. Fe deficiency can lead to greater absorption and toxicity of Cd and Pb. At low concentrations, it can reduce As poisoning through the excretion of AseSe compounds. However, excessive Se can increase As.Ca and Mg toxicity and compete with Pb or Cd for intestinal absorption to reduce toxic metal loads and prevent tissue damage caused by toxic metals competitively binding to the enzyme's active site. Essential trace metals, with their antioxidant properties at normal levels, can resist oxidative stress caused by toxic metals, thereby reducing the toxicity of toxic metals (Jaishankar et al., 2014)

Heavy metals influence CVD risk through changes in body weight. Exposure to low lead levels during development results in obesity later in life. Pb intake during development leads to higher food intake, body weight and body fat, and insulin response. Several studies reported that Hg, Mn, and Co affect lipid metabolism in adipose tissue, and Hg can accelerate the development of obesity-related diseases. Studies in humans have also found that toxic metals can contribute to weight changes and are associated

with obesity. A US NHANES study found that Ba and Tl were positively related, while Cd, Co, and Pb were negatively related to BMI and waist circumference. US adults with a higher BMI have lower levels of Hg in their blood. Cd levels in adults were found to be negatively associated with being overweight. Overweight/obese women were found to have a high prevalence of Ni allergy, and a low Ni diet may help with weight loss (Genchi et al. 2017). Display Toxic metals can also increase the risk of hypertension. The effect of Pb on increasing blood pressure has been consistently reported, and exposure has also been associated with hypertension (Sevim, 2017).

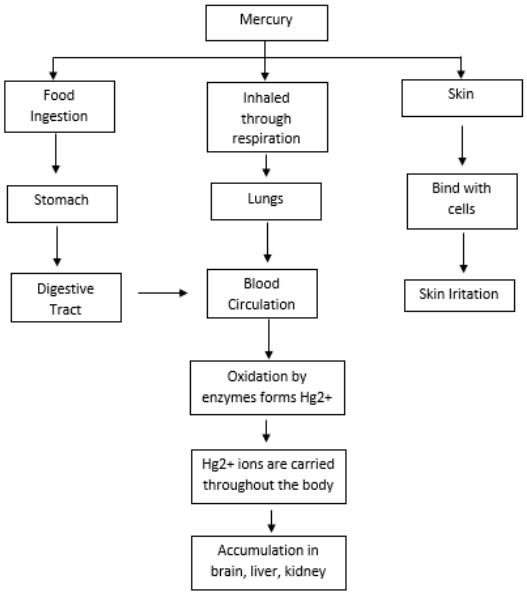
5. Mercury and Cardiovascular Disease

Mercury is one of the most toxic heavy metals and has no known physiological role in humans. Different entry routes for mercury (air, water, food, vaccines, drugs, and cosmetics) result in its easy accessibility to humans. In particular, in populations whose diets are primarily based on fish consumption, the risk of mercury exposure increases. In many developing countries, mercury is still a big problem. Various efforts must be made to reduce the use of mercury globally. Exposure to mercury and its compounds has resulted in harmful effects on human health. Mercury and methyl mercury induces mitochondrial dysfunction, decrease ATP synthesis, deplete glutathione, and increase phospholipid, protein, and DNA peroxidation. Selenium and fish, rich in omega-3 polyunsaturated fatty acids, fight mercury toxicity (Pratiwi et al., 2020).

The vascular effects of mercury include increased oxidative stress and inflammation, reduced oxidative defenses, thrombosis, mitochondrial dysfunction, depolarization, and your car's inner mitochondrial membrane. Another mechanism by which mercury exerts a toxic effect on the cardiovascular system is the inactivation of paraoxonase, which causes HDL dysfunction to reduce cholesterol transport back to the liver. This enzyme is an important LDL antioxidant, so it is directly involved in atherosclerosis, myocardial infarction, and cardiovascular disease. Mercury toxicity strongly correlates with hypertension, coronary heart disease, myocardial infarction, cardiac arrhythmias, carotid artery obstruction, cerebrovascular accidents, and general atherosclerosis (Pratiwi et al., 2020). Mercury can bond with other compounds such as chlorine, sulfur or oxygen. These bonds will form inorganic mercury compounds or salts. Most inorganic mercury compounds are powder or a white solution except mercury sulfide (cinnabar). Cinnabar It has a red color and turns black when exposed to light. Mercury is commonly found in nature in the form of metallic mercury. Mercury sulfide, mercuric chloride and methylmercury ((Pratiwi et al., 2020).

The release of mercury from natural sources has remained the same over the years. However, the mercury concentration in the environment has increased due to human activities. Most of the mercury from human activities is released into the air by burning fossil fuels, mining, smelting and burning solid waste. Several human activities cause the release of mercury directly into the soil or water, for example, the use of fertilizers and disposal of industrial waste. All mercury released in the environment ends up in the soil or surface waters. Mercury is not found naturally in foodstuffs. However, mercury can appear in food because it is spread in the food chain by small organisms consumed by humans, such as fish. Mercury concentration in fish usually exceeds the concentration in water. Farm beef products can also contain mercury. Mercury is generally not found in plants but can enter the human body through vegetables and other plants. This can happen when pesticides contain mercury (Sudarningsih, 2021).

Figure 3. Mercury Toxicity Mechanism[3]



In recent years, mercury's toxic effects have been associated primarily with the central nervous system, kidneys and brain; however, mercury can also cause cardiotoxicity. It was reported that exposure to mercury compounds, caused by frequent fish consumption by a population of the Amazon basin in Brazil, strongly correlates with increased arterial blood pressure. Studies of BP and heart rate variability among an aboriginal population from Quebec, indirectly exposed to mercury and methylmercury, have been reported by Valera and coauthors. This study demonstrates the deleterious effects of mercury and MeHg on BP and HRV in Inuit adults. At the same time, exposure to MeHg during childhood affects HRV among Inuit Nunavik children regardless of BP. Thurston et al. reported that prenatal exposure to MeHg from seafood consumption increased children's blood pressure. Grandjean et al. studied whether heart function in childhood is affected by exposure to MeHg from seafood (Sudarningsih et al., 2021).

Display Methyl mercury associated with decreased low-frequency sympathetic and high-frequency parasympathetic modulation of HRV. Other studies have linked exposure to toxic mercury with an increased risk of myocardial infarction, atherosclerosis, hypertension, and coronary dysfunction. Mercury levels in hair are predictors of oxidized LDL (low-density lipoprotein) levels, frequently found in atherosclerotic lesions and associated with atherosclerotic disease and acute coronary insufficiency. The toxic effects of mercury in all its forms have been demonstrated in vitro in animals and humans. Mercury exposure increases the production of free radicals, reactive oxygen species (ROS), and superoxide anions due to the Fenton reaction. Mercury binds to molecules containing thiols (-SH) and selenium, forming selenium-mercury complexes and reducing glutathione activity. Peroxidase, catalase, and superoxide dismutase are due to the absence of selenium at the active sites of these enzymes. Increased ROS and decreased antioxidant enzyme activity increase the risk of developing cardiovascular disease. In addition, mercury increases LDL oxidation and destroys the integrity of plasma membrane phospholipids by externalizing phosphatidylserine. In addition, the translocation of phosphatidylserine from the inner to outer mitochondrial membrane leaflets leads to modification of the mitochondrial membrane with loss of mitochondrial potential and apoptosis. As a result, mitochondrial function changes, and mitochondrial permeability transition (MPT) is affected by reduced membrane potential, oxidative phosphorylation, and ATP production (Jaishankar et al., 2014).

Another mechanism by which mercury is responsible for its toxic effects on the cardiovascular system is the inactivation of paraoxonase, an extracellular antioxidant enzyme associated with HDL (high-density lipoprotein). Paraoxonase inactivation causes dysfunctional HDL to reduce reverse cholesterol transport. This enzyme also plays an important role as an LDL antioxidant. This process is directly involved in developing atherosclerosis and the risk of acute myocardial infarction, cardiovascular disease, coronary heart disease, and carotid artery stenosis. Mercury, in mammals, activates phospholipase A2 which contributes to the development of several inflammatory diseases associated with coronary artery disease, acute coronary syndromes, and cerebral plaque rupture. Phospholipase A2 catalyzes the hydrolysis of glycerophospholipids at the sn-2 position, producing acid-smooth phosphatide and arachidonic (Genchi, 2017).

Human mercury exposure is linked to anthropogenic activity. Mercury was one of the earliest elements discovered to be non-essential for biological processes and was considered toxic due to its accumulation in organisms. Mercury affects neurological, renal, respiratory, immunological, dermatologist, reproduction and development. Mercury toxicity varies depending on the chemical forms involved and the route of exposure. Mercury induces oxidative stress, which causes membrane damage, enzymatic damage and oxidation of biomolecules. Mercury exposure decreased the catalytic activity of GPx and promoted the synthesis of H2O2 and lipid peroxidation (LPO) products (Yorifuji, 2018).

Mercury induces oxidative stress, which causes membrane damage, enzymatic damage and oxidation of biomolecules. Mercury exposure decreased the catalytic activity of GPx and promoted the synthesis of H2O2 and lipid peroxidation (LPO) products in the kidney membrane and mitochondria. Thus, mercury stimulates the production of malondialdehyde (MDA), 4-hydroxy alkenes (4-HOA) and advanced protein oxidation products such as tyrosine, which increases the inflammatory response (Flores et al. 2019).

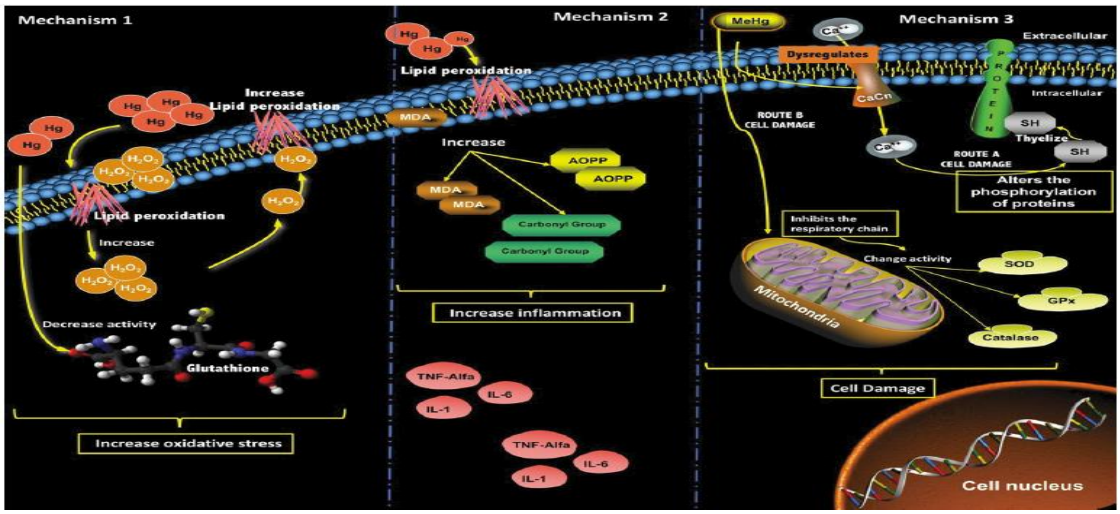


Figure 4. Mechanism of Mercury Induced Oxidative Stress[12]

According to a study by Salonen et al., mercury levels in hair and fish intake are positively associated with an increased risk of acute myocardial infarction and death from cardiovascular disease and coronary heart disease. This relationship is due to the effects of very high mercury-catalyzed lipid peroxidation. Contaminated fish in that region (Chowdury, 2018).

One case-control study found a positive association with non-fatal myocardial infarction was retrospective and had a higher participation rate among cases. Thus, selection and recall biases may occur that affect the results. A prospective study found a positive association with coronary disease events but no dose-response relationship and no association with overall cardiovascular mortality. Two cross-sectional studies found a positive association with cardiovascular disease and another with arterial stiffness. However, the cross-sectional design could not establish causality, and both studies measured blood rather than toenail mercury concentrations. Blood samples do not hold up as well as fingernail samples; red blood cells usually have a turnover of 17 weeks, compared to 26-52 weeks for toenails (Min et al. 2020).

Study Chowdhury et al., 2018, and Downer et al. 2017 yang show that the absence of an association between mercury exposure and increased risk of cardiovascular disease in adults should not change ongoing public health and policy efforts to reduce mercury contamination in fish and the environment, which still has the potential to offset, at least in part, nets. Cardiovascular benefits of fish consumption. These findings should not change recommendations aimed at pregnant or breastfeeding women; exposure to methylmercury from consuming certain fish species can cause neurodevelopmental damage (Downer, 2017).

Even in populations that consume fish, the risk of mercury exposure increases, important evidence from experimental studies in humans shows that consumption of even small amounts of fish and seafood significantly reduces heart disease and death. Selenium and fish rich in omega-3 polyunsaturated fatty acids can fight mercury toxicity. Fish consumption can balance the toxic effects of mercury with the benefits of omega-3 polyunsaturated fatty acids. Mercury toxicity should be evaluated in every patient with hypertension, coronary heart disease, cerebrovascular disease, or other vascular disease and with a history of exposure or clinical evidence of mercury excess (Genchi, 2017).

6. Conclusion

The presence of heavy metals is still a health risk in wetlands. The results of the 2020 study on the heavy metal content in the sediments of the Martapura River in South Kalimantan, which have passed the threshold for sediment contamination, include Mn, Fe and Hg. Metal content that crosses this threshold, especially mercury (Hg), can be a cause or a risk factor for cardiovascular disease. The effects of heavy metal content, such as mercury, on health, especially cardiovascular disease, are still not fully understood, requiring further investigation and research.

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