Spanish Journal of Innovation and INTEGRITY
ISSN: 2792-8268
Volume: 41, Apr-2025
http://sjii.indexedresearch.org

Pathological Conditions Occurring in the Thymus as a Result of Exposure to Heavy Metals Such as Chromium, Mercury, Arsenic, And Nickel

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Abstract: *This article provides a comprehensive analysis based on scientific research, experimental models, and clinical observations of the impact of heavy metals distributed in the environment of industrialized societies on the human body, particularly on the thymus — the central organ of the immune system. According to the research results, chromium, mercury, arsenic, nikel, and other heavy metals cause oxidative stress, inflammation, apoptosis, and epigenetic changes in cells.*

Moreover, gene regulation disorders, signal transduction disruption, and cellular mechanism dysfunction lead to immunosuppression, decreased protection against infections, and the development of autoimmune conditions.

Keywords: *thymus, heavy metals, chromium, arsenic, nikel, mercury, apoptosis, thymic involution, atrophy, autoimmune diseases, lymphoid tissue degeneration.*

Relevance: After the industrial revolution and the development of modern technologies, the amount of heavy metals distributed in the environment has significantly increased. These metals are released into the environment through industrial waste, vehicles, agricultural products, and other sources and enter the human body through various means. Some heavy metals traditionally used in textile production processes evaporate into the air we breathe or are absorbed through our skin. Some of them may be carcinogenic or affect fetal development, while others may trigger allergic reactions in humans. Long-term exposure to heavy metals has serious negative effects on human health. It causes numerous severe health problems such as kidney failure, cancer, and others.

Materials.

The thymus is considered the main organ ensuring the development and activity of the immune system in the body. The thymus ensures the normal development and differentiation of T cells (thymocytes). T-lymphocytes are the main defense mechanism against pathogens. Scientific studies have shown that when the thymus functions normally, the total number and composition of T-lymphocytes remain balanced. Through the thymus, specific restoration and selection mechanisms are carried out in the immune system to prevent non-autogenic reactions and autoimmune conditions. These processes, including positive and negative selection, play an important role in strengthening immune responses against pathogens. The thymus in a normal state plays a crucial role in the formation of a quick and effective immune response to infection in the body. Several experimental studies have shown that when

thymus function is impaired, immune responses against infections decrease and susceptibility to diseases increases. Under the influence of heavy metals, significant disruptions in these processes are observed in the thymus.

Research and methods.

Chromium (Cr). Chromium (Cr) is a heavy metal widely used in industry, and its hexavalent form (Cr^{6+}) is considered toxic to the body. When it enters the body through the respiratory tract, skin, or food, it causes serious damage to the immune system, particularly the thymus. When working with chromium, protective equipment must be used (masks, gloves, special clothing).

When poisoned with chromium, increased apoptosis, thymic atrophy, degeneration of thymic cells, and tissue remodeling also occur. Among thymic cells, stress proteins (p53, Bax) increase, and the apoptosis process is activated. Thymic fibrosis (excessive growth of connective tissue) is observed, which reduces its function and eventually causes complete loss. As with other heavy metal poisoning, a decrease in the number of T-lymphocytes and weakened immunity are observed.

Chromium exposure, like that of other heavy metals, causes oxidative stress. Chromium depletes glutathione reserves and sharply increases the amount of reactive oxygen species. This leads to lipid peroxidation and protein denaturation in thymic cells.

DNA fragmentation: Chromium binds chemically to DNA, forming cross-links. This inhibits the activity of enzymes that repair DNA errors, stopping T-lymphocyte maturation.

Thymic atrophy: Lymphoid tissues decrease, and thymus volume reduces. This results in deficiency of $CD4^+$ and $CD8^+$ T-lymphocytes.

Cancer risk: DNA damage in the thymus may lead to the development of lymphoma or leukemia.

Mercury (Hg). Mercury (Hg) is considered a highly toxic substance for the body. Thymic mercury poisoning also disrupts the maturation and differentiation processes of T-lymphocytes. Mercury affects the endocrine system, leading to thymic shrinkage and disruption of immunity.

Like chromium, mercury suppresses the activity of antioxidant enzymes (glutathione peroxidase, superoxide dismutase), resulting in increased reactive oxygen species and free radicals that damage thymic cells. Apoptosis markers (p53, Bax) are activated, slowing the growth of T-lymphocytes. Gaps form in the cortical and medullary layers of the thymus, disrupting immune balance. Cytotoxic T-lymphocytes become improperly activated and attack their own cells.

Increased production of autoantibodies leads to the destruction of one's own cells, increasing the risk of developing autoimmune diseases such as rheumatoid arthritis, scleroderma, and multiple sclerosis. Epithelial cells undergo necrosis, which results in thymic dysfunction.

Activation of glucocorticoid receptors: Organotin compounds exert effects similar to cortisol, activating apoptosis in thymic cells. This causes rapid loss of lymphoid tissues.

Defects in T-lymphocyte differentiation: The $CD4^+/CD8^+$ ratio in the thymus is disrupted, and the balance of the immune response is lost.

Increased inflammation: Mercury activates the NF-κB pathway, increasing mediators such as IL-1β and TNF-α. This leads to chronic inflammation and fibrosis of the thymus. As with chromium poisoning, connective tissues develop in place of lymphoid and epithelial cells in the thymus (fibrosis). As a result of fibrosis and sclerotic changes, the thymus may completely lose its function. Chronic inflammatory processes may cause thymic degradation.

Hormonal imbalance: Since thymic function is regulated hormonally, mercury's endocrine effects cause long-term immunosuppression.

Arsenic (As). Arsenic (As) is a highly toxic element that enters the body through water, food, and air, causing damage to various organs, including the thymus. Inorganic forms of arsenic (e.g., arsenite) halt mitosis in thymic cells and disrupt the immune system.

Mitochondrial dysfunction: Arsenic disrupts ATP synthesis, leading to energy deficiency in cells.

Disruption of DNA methylation: Gene expression in thymic cells changes, halting the differentiation of lymphoid progenitor cells.

Increased inflammation: Activation of the NF-κB pathway leads to elevated levels of mediators such as IL-6 and TNF-α.

Thymic fibrosis: Similar to chromium and mercury poisoning, connective tissues displace lymphoid elements, resulting in loss of thymic immune function.

As in cases of copper, mercury, and chromium poisoning, apoptosis markers (p53, Bax) are activated, leading to a decrease in T-lymphocytes and weakening of the immune system.

To protect against arsenic-contaminated environments, it is necessary to monitor the composition of water and food.

Nickel (Ni). Nickel (Ni) is often used in jewelry, medical instruments, and industrial products. It has a strong effect on the immune system, causing improper activation of T-lymphocytes through the thymus. Nickel poisoning leads to a disruption of the Th1/Th2 balance and, as with other heavy metal poisonings, causes allergic reactions.

Th1/Th2 imbalance: Nickel activates Th2 cells, leading to excessive production of cytokines such as IL-4, IL-5, and IL-13. This results in allergic reactions and the development of autoimmune diseases.

Damage to thymic epithelial cells: Nickel activates inflammatory signaling pathways (NF-κB) via TLR-4 receptors on the cell membrane, causing necrosis of thymic epithelial cells.

Fibrosis and loss of lymphoid tissue: Inflammatory mediators (TNF-α, IL-6) stimulate the growth of connective tissue, reducing the immune function of the thymus.

Reduction of T-regulatory cells: The number of $CD4^+$, $CD25^+$, $FoxP3^+$ T-cells decreases, impairing immune tolerance, and the body begins to attack its own tissues.

Scientific studies have recorded up to a 20–25% reduction in thymus mass and a decrease in the total number of T-cells by up to 25% in areas where cadmium concentrations were 0.05 mg/L and mercury concentrations were 0.002 mg/L.

In experimental models, animals exposed to heavy metals showed a marked reduction in protection against infections, the development of autoimmune reactions, and the appearance of epigenetic changes.

Data obtained through gene regulation, DNA methylation, and histone modification confirm the existence of significant differences in thymic cells exposed to metals compared to normal conditions.

Recent studies have tracked changes in new biomarkers and gene expression dynamics, providing opportunities to further elucidate the molecular mechanisms of immune process disruption associated with heavy metal exposure.

Damage to the thymus is especially dangerous in children and adolescents, as the thymus plays a critical role in immune system development during this period. For thymus function restoration, proper nutrition, physical activity, and stress reduction are important. Therefore, joint implementation of comprehensive measures such as environmental monitoring, food safety, antioxidant and chelation therapy is essential.

Results and discussion.

To prevent heavy metal poisoning, it is necessary: To avoid sources of environmental pollution. To prevent poisoning, it is necessary to regulate ecology, use personal protective equipment (masks, gloves, special clothing), and apply effective detoxification methods. It is very important to follow preventive measures and to eliminate toxins from the body in a timely manner. To strengthen the immune system, antioxidants (e.g., vitamin C, vitamin E, selenium) and proper nutrition are recommended.

In case of heavy metal poisoning, detoxification can be performed under medical supervision using chelators:

1. Detoxification:

- For chromium, and cadmium: chelating agents such as DMSA (dimercaptosuccinic acid) or EDTA (ethylenediaminetetraacetic acid).
- For arsenic: dimercaprol (BAL) or DMSA (succimer).
- For nickel: D-penicillamine or EDTA.
- For chromium: N-acetylcysteine (NAC) combined with antioxidants such as vitamin C and E.
- For mercury: cholestyramine to remove water-insoluble organotin compounds.

2. Antioxidant therapy: Vitamin E, C, selenium, and glutathione preparations reduce oxidative stress.

3. Immunomodulation: Intake of substances that stimulate metallothionein synthesis, such as zinc, selenium, and vitamin D3, helps restore thymus function. Strengthening immune tolerance through probiotics.

4. Environmental control:

- Proper disposal of industrial waste.
- Monitoring, recycling, and managing waste from metallurgy, chemical industry, and other production processes according to environmental standards.
- Monitoring pollution of air and water by heavy metals.
- Reducing transport emissions.
- Continuous monitoring of heavy metal levels in food products, ensuring product quality using modern measurement methods and certification systems.

5. Personal protection: Use of personal protective equipment (masks, gloves, special clothing). When working with nickel and chromium — use of neutralizing creams and respirators.

Conclusion: As evident from the scientific literature, exposure to heavy metals causes serious pathological changes. Based on scientific research and experimental models, it has been established that heavy metals distributed in the environment have a significant impact on the normal development and functions of thymic cells. Oxidative stress, inflammation, cellular apoptosis, and epigenetic changes caused by heavy metals lead to immune system dysfunction, low resistance to infections, and development of autoimmune reactions. Disruption of gene regulation and deformation of signal pathways weaken the overall immunity of the body and reduce defense against diseases.

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