



Received: 26 April, 2022

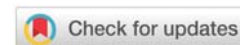
Accepted: 10 May, 2022

Published: 11 May, 2022

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Editorial

What is the consequence of metals on human health?

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The Industrial Revolution has caused increasing amounts of pollution in the environment that has exposed the global population to various agents called environmental contaminants or pollutants, which are toxic metals, as well as smoking or radiation, and may cause epigenetic modifications related to health outcomes in the later stages of life, including cancer, heart disease, kidney disease, and neurological conditions, that may be influenced by epigenetic mechanisms triggered in intrauterine and neonatal life.

Some natural substances and xenobiotics, which are chemical substances synthesized by man and released into the environment, affect the endocrine system, that is, they would act as endocrine disruptors, which are a series of persistent, organohalogenated and bioaccumulated compounds that include synthetic compounds and that continue to enter the food chain using pesticides (fungicides, herbicides, and insecticides) such as Dichloro-Diphenyl-Trichloroethane (DDT), which are now, or via ingestion in the case of plastics, with compounds such as bisphenol A and phthalate that are still found in the environment, and certain metals.

At present, negative effects of some toxins such as heavy metals are currently being detected. Heavy metals are metallic and metalloid chemical elements that are toxic to the environment and humans, and that may be present in humans. In some cases, they are essential for the maintenance of biochemical systems, but in certain amounts, they can be toxic. Exposure to metals may be due to contamination of water, due to its presence in soil or dust, fumes, or aerosols that are emitted into the atmosphere by industrial discharges, such as those related to the consumption and production of

gasoline. Certain characteristics such as easy assimilation and bioaccumulation in organisms mean that they represent a potential risk to human health, especially when consuming contaminated food. Their concentration in the environment, in water, as well as exposure time, pH, temperature, salinity, and intrinsic factors (body mass index: BMI, gender) can influence the accumulation of heavy metals in the organism.

Among their detrimental effects are the interaction with essential metals due to electronic similarity, the formation of metal-protein complexes with inactivation of their function, the enzymatic inhibition of proteins with sulfhydryl groups, and the affectation of cellular organelles: mitochondria, lysosomes, and microtubules.

As regards effects on reproduction, sperm counts decreased in the last thirty years. There are many factors affecting semen production, such as stress, trauma, obesity, nutrition, tobacco smoking, and chemical substances like polychlorinated biphenyls and saturated fats. In addition, attention has also been paid to ethnic, genetic, and environmental factors, prenatal chemical and adult pesticide exposure, environmental pollution, occupational exposure, and changes in habits or lifestyle, all of which have been the subject of extensive research.

Xenobiotics and other factors such as radiation, can act directly on the germ cells of the mature testicles, but they can also act indirectly, through the exposure of the woman during pregnancy, altering the development of the reproductive tract in the male, in such a way that it affects the germ cells and the somatic tissue producing testicular dysgenetic syndrome,

characterized by poor seminal quality, hypospadias, testicular cancer, and cryptorchidism.

Of these toxins, pollutants, or metals, some can affect sperm quality, such as Cadmium (Cd), Lead (Pb), Zinc (Zn), and Iron (Fe), among others. It has been observed that Cd and Pb are two of the metals that exert a greater influence, with increased amounts being found in infertile men with a significant inverse correlation between concentration and sperm motility and count in oligoasthenozoospermic men.

However, some elements are considered essential, these are called essential metals. Therefore, a distinction can be made between Copper (Cu), Chromium (Cr), Manganese (Mn), Zn, Cobalt (Co), Fe, and the Vanadium (V), compared to Cadmium Cd, Mercury (Hg), and Lead (Pb) which are toxic.

These changes in seminal samples appear to be relatively recent and could be related to lifestyle or the increased concentration of pollutants and environmental toxins in developed countries. Evidence from toxicological, epidemiological, biochemical, and physiological studies shows that toxins and pollutants have adverse effects on human health and can cause male infertility, either by affecting endocrine function or spermatogenesis.

In conclusion, the detection of metals in semen opens up a new field in the study of male infertility, and many cases of unknown infertility might be due to the presence, absence, or alterations in the proper concentration of metals in semen, with the opportunity of providing treatments for these possible anomalies. No relationship has been found between spermogram, sperm motility, and concentration with non-essential metal levels, although Ni levels tend to be lower in patients with oligozoospermia. The occupational exposure factor has a significant effect on metal concentrations in sperm as patients with occupational exposure to metals have a lower sperm concentration. There is a significant relationship between the level of occupational exposure to metals and Ni and an increase in the levels of Aluminum (Al) in the semen of workers with high occupational exposure. In addition, occupational exposure to metals and place of residence have some effects on Al and V levels in semen. No relationship has been reported between spermogram, sperm motility, and concentration with metal levels, although Ni levels tend to be lower in patients with oligozoospermia.

On the other hand, normozoospermia is related to higher amounts of Ca, Fe, and Zn than pathologic stereograms. Increased levels of Fe in human semen appear to have a significant correlation with male fertility, suggesting that Fe in human seminal plasma is an important factor in male reproductive function. Fe acts as an antioxidant being a co-factor of catalase, which protects sperm. In addition, elevated Fe levels are also associated with sperm damage and continue to increase lipid peroxidation that will affect the plasma membrane and the sperm motility. Most authors associate Fe

with sperm motility and higher estimated fertility potential, based on standard semen parameters for infertile men, which are associated with lower levels of Fe. Normozoospermia is associated with higher amounts of Fe. In males with pathological spermogram, the percentage of men with Fe in semen was lower than expected.

There are few studies analyzing the effect of heavy metals in paternal semen on ART outcomes. Therefore, more studies are needed to understand the real impact of metals on ART results. The study here confirms the importance of Zn, Fe, Ca, Na, Al, Mg, V, and Pb in the positive-negative effects on reproduction and supports the analysis of metals in semen as a new field of study on male fertility with implications for reproductive outcomes.

Moving on to the repercussions of the presence of metals on female fertility at the ovarian follicular level, patients who are unable to conceive have elevated Pb levels in the follicular fluid that will result in a decreased probability of pregnancy. Cobalt (Co) produces a decrease in the number of embryonic blastomeres, which induces worse results in reproduction, and Zn concentration produces a beneficial effect for reproduction since its high levels in blood and urine favor follicular development. In the same way, elevated levels of Cd in follicular fluid have a positive relationship with fertilization.

On the other hand, there has been an increase in the number of studies recently aimed at detecting possible alterations in the fetus's health that are related to environmental exposure to various elements. Their effects on fetal development not only can have immediate consequences but even long-term consequences for adult health. This environmental exposure can affect molecular reprogramming during the most critical periods of development, such as preconception, preimplantation, fetal period, and early childhood.

It is worth mentioning that among the most important causes of perinatal and infant morbidity and mortality in low birth weight, it has been observed that alterations in the concentrations of trace elements and minerals adversely affect the outcome of pregnancy. The presence of metals in pregnant women with premature rupture of membranes has also been demonstrated.

Regarding obesity, in obese patients (BMI ≥ 30.0 kg/m²) the percentage of men with Fe in semen is less than expected, and obesity harms seminal quality and is associated with higher rates of asthenozoospermia and oligozoospermia. In addition, obese patients have low levels of Pb in semen probably due to the accumulation of Pb in the fatty tissue.

The importance of knowing the real impact of metals on health lies in the possibility of being able to prescribe preventive and therapeutic measures for certain conditions, as well as advising certain healthy consumption habits.