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A MODERN VIEW OF THE IMPACT XENOBIOTICS ON ORGANISMS

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Abstract. Environmental pollution with toxic metals is a serious problem all over the world, due to their increasing accumulation in the food chain and prolonged circulation in the ecosystem. A large number of substances alien to humans and animals circulate in the biosphere - xenobiotics, which have a high toxicity. Heavy metal salts affect the spermatogenic and steroidogenic functions of the testicles, impair male fertility, sperm quality and cause testicular degeneration, ultimately leading to infertility. Exposure to xenobiotics leads to abnormalities of the reproductive tract, testicular cancer and infertility in men, called testicular dysgenesis syndrome. Although the mechanism of this syndrome is still unclear, since exposure to toxicants on the fetus can permanently cause male infertility in adulthood.

Key words: xenobiotics, heavy metal salts, testicles, hematotesticular barrier, cumulation, infertility, spermogram.

Introduction. Due to the intensive growth and development of industry, transport, industrialization and chemicalization of agriculture, acceleration of scientific and technological progress, in recent years, the intake of heavy metals of technogenic origin into the environment has significantly increased and continues to increase (Teplaya G.A. 2013).

According to the World Health Organization (WHO), among pollutants that have a negative impact per person, heavy metals occupy the second place, second only to pesticides and significantly ahead of such well-known environmental pollutants as carbon dioxide and sulfur (Titov A. F., 2014).

Pollution of water, soil and air with toxic metals is an environmental problem that affects hundreds of millions of people around the world. Contamination of food products with heavy metals is another problem for human and animal health. In this regard, the concentration of heavy metals in water resources, air and food products is estimated (Luo et al., 2020). Metals among other environmental pollutants can also occur in nature and remain in the environment. According to Tchounwou et al., 2012 xenobiotics often react with biological systems by losing one or more electrons and forming metal cations with affinity for nucleophilic sites of vital macromolecules.

Xenobiotics enter the body in different ways, through water, air, food, sometimes through the skin. After absorption, the toxicants are delayed and accumulate in the human and animal bodies. Bioaccumulation of toxic metals leads to a variety of negative effects on different tissues and organs of the body (Balali-Mood M., 2021).

The organs of the mammalian reproductive system include testicles (testes, testicles) – their main function is the formation of spermatozoa and the release of sex hormones (testosterone) into the bloodstream. The hematotesticular barrier is one of the densest hematotecular barriers in the mammalian body (Yan C. et al., 2012).

Some heavy metals, due to acute and chronic toxic effects, affect various organs and systems of the body. Gastrointestinal and urinary tract dysfunction, nervous and endocrine system disorders (Fernandes Azevedo et all., 2012), skin lesions (Cobbina et all., 2015), vascular damage (Costa, 2019), immune system dysfunction (Gazwi et all., 2020), birth defects of reproduction and cancer They are examples of complications of the toxic effect of heavy metals (Gazwi et al., 2020). Simultaneous exposure to two or more metals can have a cumulative and negative effect (Gazwi et al., 2020). Lead

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pollution is a consequence of industrialization and human activity. It was found that children living near lead factories in Idaho (USA) had blood lead levels of about 25 mg/dl and suffered from severe anemia. As a result, lead poisoning for a long time can cause reproductive dysfunction (Giuliani R., 2005).

According to the Agency for Toxic Substances and Disease Registry, (2020), lead is on the list of the most dangerous environmental poisons. Lead is widely distributed in nature, presented in the form of lead sulfide or chloride.

Exposure to high doses of lead can cause serious complications such as abdominal pain, bloody diarrhea and kidney failure (Tsai et al., 2017). However, low doses of heavy metals pose a subtle and hidden threat, in the form of neuropsychiatric disorders, fatigue, anxiety and a detrimental effect on the intelligence quotient and intellectual function in children (Mazumdar et al., 2011).

Studies on experimental animals (rats and rabbits) have shown that lead is toxic to testicular function and tissue. Lead can interfere with the mitosis of spermatogenic cells and cause a change in the proliferation of Sertoli cells. As a result, reducing the number of spermatozoa in the testes and further reducing the number of spermatozoa in the appendages of the testicles. Corpas et al. (2002) mentions that lead acetate poisoning during spermatogenesis can delay spermiation and release of immature spermatogenic cells in the seminal tubules of the testicles.

According to Koedrith et al. (2013), some metals have become carcinogens to humans, such as cadmium, can disrupt DNA synthesis and repair.

According to Wang et al., (2006) lead can cause apoptosis of spermatogenic cells in testicular seminal tubules and has a toxic effect on testicular spermatogenic cells. But Mariola et al., (2004), Patrick, (2006) have a different opinion, who believes that the toxic effect of lead on the testicles is due to the formation of excess reactive oxygen species. There is a positive correlation between an increase in reactive oxygen species and a higher level of caspase-3 detected during apoptosis of testicular cells (Wang et al., 2003).

Vigeh et al. (2011) describe the ability of lead to increase the amount of reactive oxygen species and inhibit antioxidant enzymes and damage to deoxyribonucleic acid (DNA). These changes are consistent with the data of Khaki and Khaki (2010), which showed that there is a significant correlation between reactive oxygen species with increased DNA damage and apoptosis of liver cells of Wistar rats exposed to lead acetate.

With the widespread use of cadmium-related products in industrialized countries, its dangerous effects are increasing. Cadmium accumulates in the human body in large doses, acts on osteomalacia, has hepatotoxicity, renal toxicity, neurotoxicity and also leads to infertility and cancer (Benoff S., 2000).

The most frequently manifested effects of cadmium exposure on reproductive organs are degenerative atresia of primordial and growing follicles, the formation of large, functionally active yellow bodies or rare ones in the regression stage, the formation of cyst–like structures (Kolosova I. I. 2013).

According to Zhu Q. (2020) in humans and mammals, cadmium causes damage to the testicles of males. It causes serious structural damage to the seminal tubules of Sertoli cells and the hematotesticular barrier, which leads to the loss of sperm. It prevents the development of Leydig cells, inhibits the function and causes tumors of these cells, also disrupts the vascular system of the testicle

In experimental studies, Yang H.S. (2006) proved that the morphology of the testicles depends on the dose of the toxic effect of cadmium. According to the author, the dose of cadmium interstitial cells were destroyed, which lead to irreversible loss of spermatogony and destruction of the basement membranes.

According to A. F. Titov (2011), aluminum is the most common metal in the lithosphere, accounting for 8% of the earth's crust. Aluminum gets into food from various environmental objects – water, household items (bags, dishes), aluminum containing food additives. In unprocessed foods, the aluminum content is less than 5-7 mg/kg.

Studies conducted in Germany, France, Great Britain, Ireland and Spain have shown that most unprocessed foods contain aluminum (Xue Z.C. 2013). Higher concentrations of aluminum are observed in bread, confectionery bakery products, some vegetables (spinach, radish, lettuce, mash salad), mushrooms, glazed fruits, dairy composite products, boiled sausages, offal, seafood. The highest aluminum content was found in leaf and packaged tea, herbs, cocoa and cocoa products, spices (Teplaya G.A. 2013).

In the scientific works of Makutin V.A. (2014) it is indicated that aluminum, with a slight effect on the body of laboratory animals, leads to a gonadotropic effect in the testes: reduces the production of free testosterone, increases the content of immobile and morphologically pathological forms of sperm, increases the proportion of aberrant divisions and sperm with DNA fragmentation, reduces antioxidant/oxidant activity in homogenate

According to Mahshid S., et al. (2007) titanium dioxide (TiO2) as a food additive is widely used in food, cosmetics and hygiene products, is part of the shells of medicines. In nature, titanium dioxide is in solid form in the form of minerals. To date, there is very little information about the quantitative content of food additives in the shells of medicines (Zachariadis G.A. 2011).

The negative effect of titanium dioxide nanoparticles on the morphological parameters of rat testicles affects key characteristics for this structure, such as the proliferative activity of cells and their ability to differentiate organs of the male reproductive system (Morgan A.M. 2017).

Infertility is one of the urgent problems of our time, according to statistics, 15% of married couples apply due to the absence of pregnancy for 1 year. It must be admitted that in the structure of infertility, the male factor occupies 40%. This indicates the vulnerability of men in the modern world. Many times the WHO revised the norms of the spermogram, deviating towards the pathological characteristics of spermatozoa. For reasons such as allergization of the population, an increase in the frequency of inflammatory diseases, congenital pathologies, social and man-made impacts (Khairutdinov K.N. et al. 2018). The causes of male infertility are complex, and the etiology of about 50% of cases remains unknown (Kilchevsky and Honig, 2012).

Studies by Skakkebaek et al. (2001) male rats are exposed to pollutants throughout their life cycle, including the embryonic period. Environmental pollutants enter directly into the testes of adult mammals and suppress spermatogenesis, male insufficiency/infertility.

In a study by Loebenstein et al. (2019), exposure to xenobiotics leads to reproductive tract abnormalities such as cryptorchidism and hypospadias, testicular cancer and hypofertility/infertility in men, called testicular dysgenesis syndrome. Although the exact mechanism of testicular dysgenesis syndrome is still unclear, epigenetic regulation is involved, since exposure to toxicants on the fetus can permanently cause male infertility in adulthood (Skinner et al. 2015). According to El-Neweshy M.S. (2013), these changes were associated with a decrease in testosterone levels.

According to Pandya C. et al. (2012), heavy metal salts affect the spermatogenic and steroidogenic functions of the testicles, worsen male fertility, sperm quality and cause degeneration of the testicles, ultimately leading to infertility.

Intoxication with heavy metal salts, according to Manal M. Sayeda (2014), leads to histopathological lesions of the testicles, interstitial edema, degeneration and formation of intracalcular giant cells.

Physical, biological and chemical methods are widely used in the purification and removal of organic pollutants. New objects for the treatment of chronic diseases are being actively studied, as well as chelators – potentially useful agents that help in detoxification of toxic elements. Chelation is the formation of multiple coordination bonds between organic molecules and metals (Sears M., 2013).

The ways of enhancing the natural detoxification pathways of chelators – Chlorella and Fucus sp. (José J.M. et all. 2019) are considered, According to Morgan A.M. (2017), the cost of correction with the above methods for research and for executors is expensive, and the influence of detoxifiers often causes undesirable effects.

It is known that herbal treatment with biological detoxifiers is one of the reliable methods of reducing the chronic and acute toxic effects on the body of organic pollutants, including heavy metals. For example, a medicinal plant like Nigella sativa (black cumin), thanks to its effective component thymoquinone (2-isopropyl-5-methyl-1,4-benzoquinone), has a protective effect and chelating activity of organs and tissues.

Thus, the literature data on the effect of xenobiotics on organisms are contradictory, they cannot fully disclose the problems of the effect of xenobiotics on the reproductive systems of male rats in the hypodynamic state of animals.

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