Exogenous Factors Affecting Male Reproduction

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Male gonads and gametes are especially vulnerable to the effect of exogenous factors; therefore, they are considered a reliable indicator of environmental pollution. The impact of xenobiotics or radiation leads to an irreversible impairment of fertility displayed by histological changes, modulated androgen production, or compromised spermatozoa (or germ cells) quality.

heavy metals radiation endocrine disruptors mycotoxins testes spermatozoa seminal plasma oxidative stress mode of action risk factors

1. Introduction

The present society is largely focused on the creation and optimization of technological methods. This effort for financial or personalistic gain, or the process simplification of production brings along high, although on first sight, imperceptible sacrifice. The development and spread of diseases of affluence reflect the negative impact of various byproducts of industrial production or other anthropogenic activities. Accordingly, the most advanced industrial areas are usually also known for the enormous environmental pollution. The accumulation and consecutive synergism of toxicants in the living environment leads to impairment of individual physiological processes or even death [1].

Contaminants, commonly known also as risk factors, may have different characteristics depending on their origin. Physical contamination is caused by ubiquitous ionizing and nonionizing radiation. Micro-organisms and their metabolites or pollens can be considered as risk factors of biological origin. Chemical contaminants include endocrine disruptors or toxic metals [2].

Pollutants tend to accumulate in different organs and harm their functions. Poisoning or contaminant-derived diseases can be acute (episodic) or can develop over time (chronic intoxication). They are often accompanied by skin problems, breathing complications, convulsions, digestive disorders, or serious failures of the central nervous system and endocrine activity. The most terrifying effects, affecting even the progeny, are mutagenicity and carcinogenicity [3][4][5][6][7][8].

A good example of the consequence of high environmental pollution is the year to year decrease in the infertility of wild animals, domestic animals, or even humans. A negative effect of toxicants (decrease in concentration, motility, or longevity of spermatozoa) is often monitored on the individual or the group of individuals, however, the mechanism of action of toxicants on the cellular level is not studied enough. If so, most of the time only one compound is studied at a time and studies do not take into consideration the possible effect of synergism or antagonism of xenobiotics [9][10][11][12].

Previous studies imply that the exogenic effect of toxicants is strongly related to the enhanced production of reactive oxygen species (ROS) and reactive nitrogen species (RNS), resulting in the degradation of biomolecules or even apoptosis [13]. On the other hand, it is important to mention that ROS are necessary for the physiological processes of spermatozoa such as capacitation or acrosome reaction. Therefore, spermatozoa may be affected by several exogenic and endogenic factors where the determining variables are the imbalance between antioxidants and free radicals and appropriate proportion between individual components of seminal plasma [14].

2. Environmental Pollution

The pollution of the environment has a serious consequence in the endangerment of human and animal health. It is caused primarily by growing industrial production, transportation, chemical substances used in agriculture [15][16], and pharmaceutical remedies [17]. Soil contamination and thus the pollution of foods of plant origin is one of the most pressing issues in discussion about food safety on the European [18] or even global [19] level.

Gonads and gametes serve as a very sensible and reliable barometer of the incidence of risk elements in the environment. They are affected via the degeneration of seminiferous epithelium, abortion of connection with the basal membrane, defects in spermatozoa development, and generation of ROS thereby reducing male fertility [20][21][22][23]. Donkin and Barres [24] report that environmental factors along with diet and lifestyle are reflected in spermatozoa epigenetics. More important, these genetic changes may be passed on to the next generations via epigenetic inheritance. We recognize three types of contaminants that can eventually cause environmental pollution and we divide them based on their character and appearance on physical biological and chemical contaminants [2].

2.1. Physical Contamination

The Glossary of Environment Statistics issued by the United Nations Department for Economic and Social Information and Policy Analysis defines physical pollution as pollution caused by color, suspended solids, foaming, thermal conditions, or radioactivity [25]. This definition was adopted by the Organization for Economic Cooperation and Development (OECD) and is still used today [26]. Color pollution is the result of color contamination by an inappropriate arrangement of colors that induces a disorder in the perception of the visual field within the natural or urban environment [27]. Suspended solids are contaminants of the water environment in the form of microplastics. Microplastics are serious polluting agents themselves, moreover, they may have a role as pathogen carriers. Their presence in a marine environment is a threat not only to aquatic flora and fauna but also to human food safety in the form of seafood and salt [28][29].

Temperature changes in the aquatic system may also cause thermal pollution which is reflected in degraded water quality. The source of thermal pollution is frequently found in the activity of power plants. The negative effect is then shown on soil erosion or on fish that exhibit thermal shock, metabolism alterations, and reproductive dysfunction [30][31]. Another water-related contaminant causing physical pollution is foaming. Due to the appearance of the foam on the surface of the freshwater, contamination can be easily visually recognizable. Foam pollution may find a cause in the natural processes of aquaculture or anthropogenic activity. Man-made pollution is often caused unintentionally by of oil, detergent, or lignosulfonate leaks. Foam lines are formed from the surfactants which reduce the tension of the water surface and enable the foam bubbles occurrence [32].

Radiation is an extensively occurring contaminant of the environment. Radiation can be divided based on the amount of emitted energy into ionizing and non-ionizing, which determinates the power and further features of the radiation. Non-ionizing radiation causes electron excitation which can induce heat generation. Ionizing radiation possesses enough energy to induce the emission of electrons from atoms and electrons being a threat to all living organisms [33][34]. Radioactive compounds are usually the waste of nuclear power generation, production of nuclear fuels, weapons development, biomedical interests, and industrial activities. However, radioactive contaminants can also originate in nature [35]. Radiation is the only exogenous agent of the group of physical contaminants that have a direct effect on male reproduction. As the ubiquitous aspect of the modern age, radiation may be considered a serious threat based on its emitted energy, frequency, and dose of exposure (Table 1).

Table 1. The effect of non-ionizing and ionizing radiation on the most targeted sites in male reproduction.

Radiation	The Site of the Effect		
	Testis	Epididymis	Spermatozoa
Non-ionizing	• dilatated and congested blood vessels in tunica albuginea and interstitium • degenerated spermatogenic cells • diminished Sertoli cells containing numerous vacuoles, swollen mitochondria, and broken organelles • enhanced production of cytokines by Sertoli cells • germ cells arrested in pre-meiotic stages	• reduced weight of epididymis • decreased sperm count • morphological defects of spermatozoa • increased lipid peroxidation • diminished content of glutathione • degeneration of epithelium cells	• dose & frequency-dependent effect on motility • spontaneous acrosome reaction • sperm head malformations • increased DNA damage [33][44][45][46][47]

Radiation	The Site of the Effect		
	Testis	Epididymis	Spermatozoa
	• induced generation of ROS [36][37][38]	[39][40][41][42][43]	
Ionizing	• decreased testis weight • damaged seminiferous tubules • disorganized spermatogenic cells • declined number of spermatocytes and spermatogonia • induced apoptosis of spermatogenic cells • degeneration of Sertoli cells • the high appearance of swelling mitochondria • extensive ROS generation [48][49][50][51]	• the lower weight of epididymis • diminished luminal diameter • high incidence of vacuoles in the epithelium • impaired spermatogenesis • reduced sperm count • elevated apoptosis • enhanced intracellular ROS • decreased level of zinc [48][52][53][54]	• decreased motility and viability • reduced sperm count • morphological malformations • elevated intracellular ROS • down-regulated expression of tubulin • decreased content of ATP [48][50][51][52]

organisms in the environment. This includes all invasive plant and animal species, pollen, but concerning reproduction, the most frequent biological pollutants are microorganisms. Either microbes themselves or their metabolites cause air, water, soil, or food pollution [55][56][57][58]. The food chain contains numerous entries for contamination. The contamination of groceries is often associated with improper storage conditions while fresh products are considered safe and healthy. This bias is frequently promoted along with a healthy lifestyle. However, microbiological threats are present in every step of the farm-to-fork chain, including the soil, water sources, cultivation, harvesting, and processing [59]. In respect to one of the highest sources of contamination, water, the US Environmental Protection Agency identifies over 500 waterborne pathogens, including viruses, fungi, bacteria, protozoa [60]. Epidemiologists also warn against the HVAC (heating, ventilation, and air conditioning) technology and hand dryers in public restrooms when they are not regularly maintained, inspected for microbial pollution, and disinfected [61].

Male reproductive organs are prone to microbial infection and subsequential inflammations. The male urogenital tract is occupied by numerous bacteria including *Escherichia coli*, *Proteus* spp., *Enterococcus* spp., and other Gram-positive and Gram-negative bacteria. The presence of bacteria in the semen is called bacteriospermia and does not inevitably mean the pathological sign. On the contrary, the presence of *Mycoplasma* spp., *Chlamydia* spp. or other pathogenic bacteria are not appreciated. Sequela such as orchitis, epididymitis may be caused by *Brucella* spp., *Mycobacterium leproe*, *Mycobacterium leproe*, or uropathogenic *Escherichia coli*. In addition to epididymis and testis, *Chlamydia trachomotis* targets and causes inflammation of the urethra, prostate, and seminal vesicles. In certain cases, when the concentration of pathogenic bacteria is too excessive, the body responds with leukocytospermia—abnormally high concentration of white blood cells in ejaculate. The physiological regulation of this phenomenon is not sufficiently explained yet [61][62][63][64]. Some authors even did not find any or just weak associations between bacteriospermia and leukocytospermia [65][66].

Semen may be considered the vector of viral infection; however, the male reproductive system may also suffer from viral contamination. It has been documented that semen may be a host to approximately 27 viruses. This includes Adenoviruses, Ebola virus, Hepatitis virus (HPV) B and C, Zika virus, Epstein Barr virus, Human immunodeficiency virus (HIV), Mumps virus, several herpes viruses, Human T-cell lymphoma virus, SARS-CoV-2 virus, etc. [62][67][68]. Evidence on the direct effect of viruses on fertility has been reported by several studies. Some viruses affect only the spermatozoa by alteration of their motility and viability (Hepatitis B and C, SARS-CoV-2, HPV) [68][69][70]. On the other hand, the CoxsacKie virus, Mumps virus, HIV, Zika virus, HPV, Influenza virus target male reproductive organs—testis and epididymis [69][70][71][72][73]. In some cases of HPV infection, the targeted site might be just Sertoli cells. This phenomenon is called the “Sertoli cell-only” syndrome [72].

2.3. Chemical Contamination

Chemical contaminants turn into pollutants when accumulations are sufficient to undesirably affect the natural environment or to present a risk to living organisms. There are thousands of industrial chemicals identified as a hazard to humans, animals, and the environment. Therefore, governmental agencies regulate their production, storage, transportation, and disposal. Sources of chemical contamination contain agricultural activities, industrial and manufacturing activities, municipal waste, service-related activities, and resource extraction [74].

3. Mode of Action (MoA)

As listed earlier, there are three types of contaminants (physical, biological, and chemical) based on their characteristics, origin, and MoA. This implies their various effects on the functionality of organs and gametes. The biological system has its own mechanisms to prevent the toxicity of the reproductive system. The hematotesticular barrier (HTB) regulates the migration of some toxicants from blood to the testis, mature sperm chromatin is inactive and firmly coiled, defective spermatocytes are degraded and replaced. The imperfection of the HTB consists in the influx of lipophilic compounds allowing the exposure of vulnerable spermatogonia to toxicants and compromises male fertility [75]. HTB is one of the tightest barriers between blood and tissue, dividing seminiferous epithelium into the basal and apical parts. Also known as the blood–testis barrier, HTB differs from other tissue barriers by its structure, composed of tight junctions, ectoplasmic specializations, desmosomes, and gap junctions. This highly specific and unique structure provides a favorable microenvironment for meiosis and following the development of spermatids into spermatozoa [76]. Spermatogonia are localized in the basal compartment while primary and secondary spermatocytes along with round and elongating and already elongated spermatids are situated in the apical compartment [77].

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