Editorial

Environmental medicine and its impact on human health

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In this Special Issue of Frontiers in Biosciences-Landmark, we have selected 7 reviews mainly by participants at our 1sr Mexican Enviromental Translational Biomedicine meeting (December 03, 2019 at Mexico City, Mexico). This event was created with the expectation to network with Mexican scientists and overseas guest scientists interested in the field of Enviromental Biomedicine, given that enviromental pollution and human health are serious concerns which have great importance and have to be discussed. As a result of human socio-economic activity, industrial waste and pollution has increased alarmingly. These have direct and indirect effects in almost every ecosystem. No matter what their impact is, pollution affects the health of every species on this planet. Wildlife is prone to suffer the same symptoms and diseases as humans. Global warming is changing some ecosystems faster than the capability of animals and plants to adapt, leading to possible extinction of a huge number of species. Toxicity of the water, reduced oxygen concentration in deeper layers of bodies of water and difficulty in adapting to the new substances may damage indigenous fauna and flora in several ways. Among the worst and most widespread contaminants in the environment are plastics. Contacts of humans with chemicals from the environment occur via air, water, soil or food. In the past most attention was paid to the contamination of air and water. The lipophilic persistent chlorinated compounds, such as DDT, PCBs and dioxins and the heavy metals lead, cadmium and mercury are accumulated in livestock and are there leading to much higher concentrations than in the environment. A range of environmental chemicals coming from the air acts directly on the site of first contact through potentially cytotoxic actions. For many of them the margin of safety is low or even non-existent. Particularly, plastics have great practical value, and this has allowed them to be readily accepted by the consumer society to the point that they are now present in many of the everyday products we use. Part of the success of plastic materials is that they are inexpensive, light and resistant. However, their resistance to corrosion and degradation makes them slow to decompose, leading to a great environmental problem. It was believed that plastics did not react with anything, that is, that they were stable, inert and therefore did not contaminate; that is not true. Unfortunately, plastics make up between 60% and 80% of the litter present in the marine environment. The wind acts on the surface of seas and oceans, acting as the engine to spread litter over these waters. The currents manage to collect all kinds of garbage in their path and finally form what are known as garbage islands or plastic islands. All of this concerns are discussed here by different authors in this Special Issue related to Environmental Medicine and Health.

The first paper, by Arteaga-Silva *et al.* [1], considers that in industrialized countries, the use of Cadmium (Cd) is a form of anthropogenic pollution. Hence, exposure of human populations is becoming a public health problem. With a half-life of up to 40 years, Cd is now a topic of great interest due to its role as an endocrine disruptor and its effects on male reproduction. Cd's diverse toxic mechanisms are based on its capacity to mimic divalent ions—calcium, zinc, iron—that participate in physiological processes. It alters mitochondrial function and generates free radicals that can induce apoptosis. In male reproduction, Cd alters the precise coordination of the hypothalamic-hypophysis-testicular axis (HHT), resulting in the loss of testicular functions like steroidogenesis, spermatogenesis and the onset of puberty, sexual maturity, sexual behavior and fertility. Exposure to Cd may even cause changes in the immune system that are associated with the reproductive system. This review analyses the state of the question regarding Cd's cellular and physiological mechanisms and the effects of this heavy metal on the neuroendocrine regulation of male reproduction. Aguilera *et al.* [2], discuss their concerns re-

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garding heavy metals in street dust, which has increased in recent decades and are worrisome due to toxicity, persistence and bioaccumulation, representing a risk to human health. The aim of their study was to review the state of the art on the human health risks of heavy metals in street dust in 39 cities of the world, basws on the US Environmental Protection Agency (USEPA) assessment. The results showed that there is contamination worldwide due to *As*, *Cd*, *Cr*, *Cu*, *Hg*, *Mn Ni*, *Pb* and *Zn* in street dust as judged by their median values exceeding the soil background values. Even when no risks of developing adverse effects for human health were identified, according to the medians of the hazard risk index, *As*, *Cr* and *Pb* had the highest values. *As* was also in the "tolerable risk" zone contributing to cancer in children and adults, as was Pb for children. The review highlighted the relevance of heavy metals in street dust for human health and will serve as a guideline for future studies in the field. On the other hand, related to microplastics, Gomez-De león *et al.* [3], delve into the endocrine disruptor contaminant bisphenol A (BPA). BPA it is an endocrine-disruptor compound with estrogenic activity. It is used in the production of materials in daily use, such as polycarbonate plastics, epoxy resins and dental sealants. The endocrine modulating activity of BPA and its effects on reproductive health have been widely studied. However, BPA effects on the immune system function have been less well-studied and the available data are inconclusive. This can be attributed to the enormous variety of animal models and the different BPA doses examined. Moreover, most studies of BPA effects on immune responses are *in vitro* and *in vivo* studies focusing almost exclusively on the impact of BPA on numbers and proportions of immune cell populations, without evaluating effects on actual immune function in response to an antigenic challenge or infection. In their review, the authors discuss the current literature evaluating the effects of BPA exposure on immune system functions and their potential role in determining susceptibility to infection. The conclusion is that BPA may act in most of the studied models as a pro-inflammatory stimulus. This makes BPA a double-edged sword, because in cases in which inflammation is related to the pathophysiology of a certain disease, the outcome it is not good but if the inflammatory response helps to control or contain that specific disease, then the prognosis is good. Next, Del Rio Araiza *et al.* [4], discuss that the communication between neuroendocrine and immune systems maintains a bidirectional complex network. Both systems jointly act during a parasite infection to maintain homeostasis and to eliminate the pathogen. Parasites interfere with the synthesis, secretion, metabolism, action, and elimination of endogenous hormones, as well as with the immune system in the host. Thus, the authors aimed to address how parasite colonization disrupts the normal homeostasis of endocrine organs of the host, likely due to the exacerbated immune response, or by the impact of the parasite directly affecting endocrine tissues. In the case of other pollutants, such as the organophosphorus compounds (OPs), Monroy-Noyola *et al.* [5] point out to they are being used in the manufacture of insecticides and nerve agents. Some commercial OPs are racemic mixtures that present at least one chiral center in the phosphorus atom. Acute exposure of humans to these racemic mixtures induce adverse neurological effects known as the cholinergic syndrome and organophosphate-induced delayed polyneuropathy syndrome, which are associated with the covalent modification of acetylcholinesterase (AChE) and neuropathy target esterase (NTE). The stereoselective interaction of the racemic OPs on these B-esterases (AChE and NTE) is related to the irreversible neurological effects, while its stereoselective hydrolysis by A-esterases or phosphotriesterases (PTEs), which include the PTE from Pseudomonas diminuta, and paraoxonase-1 from human serum (PON1) has been studied *in vivo*, *ex vivo* and *in vitro*. Bacterial PTE has shown a significant catalytic activity on the less toxic isomers P (+) of the nerve agents; meanwhile, PON1 presents a limited hydrolysis capacity of the racemic OPs. Thus, the authors discuss that these proteins have been subject of study in biotechnology, and the design and production of recombinants could be used as bio-scavengers in clinical toxicology and biocatalysts in environmental bioremediation for OPs. Other proteins, such as avian serum albumin, have demonstrated a hydrolyzing capacity for chiral OPs with oxo and thio forms, and can also be used to this end. Palacios-Arreola *et al.* [6], review another microplastic component, phthalates. These are endocrine disrupting compounds (EDCs) used as plasticizers in a wide array of daily-use products, from flooring and automotive parts to medical devices, and are even present in children's toys. Since these compounds are not covalently bound to other molecules, they leach from these synthetic products, causing a high level of human exposure to them. EDCs exert several endocrine effects, most typically, reduced biosynthesis of testosterone and disturbances in estrogen, androgen, PPAR-gamma and AhR that control complex immunoendocrine regulatory networks. Besides impacting on developmental processes and mediating long-term adverse effects, because cells of the immune system express endocrine receptors, and synthesize and respond to several hormones and other endocrine ligands, phthalates also cause dysregulation of the immune system. Finally, Rebolledo-Solleiro *et al.* [7] delve into the neuroendocrine effects of BPA. Numerous studies have reported a variety of effects of BPA in animal models and clinical studies, including alterations in the reproductive system (for example, fertility problems, ovarian cysts, damage to testicular histoarchitecture, prostate cancer), metabolism (obesity), brain functions and, consequently, behavior. It has recently been proposed that exposure to BPA may be associated with the development of certain neurodegenerative diseases and neurodevelopmental disorders. However, it is a line of research that is just emerging and with many questions still

to be resolved. The aim of their contribution was to review the available information about the association between exposure to BPA and cognitive function, behavioral disturbances, neurodegenerative diseases (Parkinson's Disease, Amyotrophic Lateral Sclerosis, Multiple Sclerosis) and neurodevelopmental disorders (Autism Spectrum and Attention-Deficit/Hyperactivity Disorders). Likewise, the molecular and cellular mechanisms that may be involved in this association are analyzed.

We hope our readers find this Special Issue enticing and enjoy reading all the contributions.

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