Adequate pollution management - a must for implementation of 'One Health' concept

https://doi.org/10.21698/rjeec.2020.109 *Review*

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Abstract

The paper focused on the possible links among pollution, pollution management efficiency including waste management and the propensity of a variety of emerging diseases in our society by answering the question: "How pollution can affect human health?" Environmental pollution is a reality and our planet ecosystem possibilities to face the challenges due to the constant exceeding its resilience are becoming smaller and smaller. The evolution of the climate change indicators like global temperature, global CO_2 emissions, oceans acidification and species extinction point out that in a not very long period of time, the planet will not be able to sustain any more the present society's life style set by the current economic development. Therefore, many warning signals have been issued to change the present behavior in order to reduce significant damages done to the environment and on human health with serious implications on the dysregulation of our immunity and the onset of a plethora of diseases. In this respect, the present paper reviewed relevant aspects linked to the environmental pollution issues that become part of scientific and public debates presented in specialty literature in recent years emphasizing why the implementation of "One Health" concept is necessary.

Keywords: *immunity, one health, waste management*

ONE HEALTH CONCEPT FROM ANTHROPIC ACTIVITIES TO POLLUTION AND SPECIES ADAPTATION SURVIVING MECHANISMS

The Senate of the United States in the 116th Congress 1st Session, January 2020 [1] defines the concept of "One Health" as being *"... a collaborative, multisectoral, and transdisciplinary approach, working at the local, regional, national, and global levels, with the goal of achieving optimal health outcomes recognizing the interconnection between people, animals, plants, and their shared environment. (...) The increasing threats posed by emerging diseases shared between animals and people, foodborne, vector borne, and waterborne diseases, and other environmental factors may support the need for an integrated effort by professionals from multiple discipliners, including health, science, technology and engineering…"*.

The global view of "One Health" concept puts together multidisciplinary obtained research data to give an important feedback to the implemented programs, policies and legislation designed to protect and improve the human health.

Unfortunately, most of the beneficial anthropic activities triggered by the human population and industrial growth have another "medal" side, namely the exhausting of the environmental non-renewable or hard renewable reserves and generating in the same time large amounts of pollutants that become a real threat for environment and human health. The overall "One Health" picture emphasizes that anthropic activities generate the greenhouse effect and subsequently climate change which beside other effects has increased the oceans temperature, allowing the *Vibrio* population (*Vibrio cholerae, Vibrio vulnificus* and *Vibrio parahemolyticus)* to raise at a life-threatening infection level for marine species and also for humans [2].

In their striving to survive, species adapt themselves to the polluted environment and this can directly affect the human health. Although, from the beginning of the last century the average human life span has substantially and continuously increased due to antibiotics and other drugs discovery, unfortunately the pathogenic microorganisms are also continuously adapting to the new antibiotics and drugs. This is a phenomenon leading to a multiple drugs resistance generating a *"red queen effect"* materialized in a microorganisms' adaptation competition to new types of antibiotic production in order to survive. The microorganisms' adaptation became a human health issue due to their generated antibiotic resistance and the associated flourishing of nosocomial diseases phenomenon. In spite of

focussing on the human health, the whole biosphere have been affected by the anthropogenic activities and over 70 % of the diseases are common for the human and animals" as it was mentioned during *The 2nd European Conference One Health in its Final Report from June 2019*, regarding the measures for regulated, coherent and sustainable application of the global concept "One Health" in Education, R&D, Medical, Economic and Social Life [3]. Despite the major morphological differences between species, at the molecular level those differences become insignificant. A family of gene encoding the so-called ABC transporters proteins is an example of high homology between species. Being one of the oldest gene families in both prokaryotic and eukaryotic cells, this is also a well-known example of their involvement in the development of multidrug resistance for both antibiotics and cancer drugs [4-6]. Genome sequencing and phylogenetic analysis of those transporters demonstrated their common evolutionary origin [4] triggering a *"correlation between evolutionary relationships of different organisms including humans and the environments in which they inhabit"* in order to adapt and survive. For example, the LmrA transporter, an ABC transporter based on ATP present in *Lactococcus lacis* is a well known entity to be involved in the mechanisms of the antibiotic resistance by pumping the amphiphilic compounds outside bacterium. It has also a homologous counterpart in *Homo sapiens* namely the P-glycoprotein which is also an ATP-based ABC transporter involved in the resistance of tumor cells to chemotherapy [7]. Due to the increased homology between bacterial LmrA and human P-glycoprotein, LmrA bacterial genes have been inserted into fibroblast cells. The generated effect was a resistance comparable to that produced by P-glycoprotein. Moreover, P-glycoprotein-specific inhibitors also retain their inhibitory properties on LmrA [8]. The overall information showed that these genes of different origins are interchangeable and demonstrates that the mechanism of resistance induced by efflux pumps has been conserved from bacteria to humans. Those cell exporters' entities act like a cellular defense mechanisms. "One Health" implementation concept relies on multidisciplinary approaches to understand the complexity of defence and adaptation mechanisms to the new and continuous environmental changes. In human evolution, the defence and adaptation mechanisms have been in the first line in ensuring the human survival in various environmental conditions, including interspecies interactions throughout the trophic pyramid. Once the pollutants brake different first defense barriers that our body has in order to protect its anatomical integrity (e.g. skin, mucous membranes) it mobilizes the defense mechanism at the site of the entrance/injury, to eliminate them from the body. In relation to these defense mechanisms, we should mention that a set of special types of molecules guard our cells by recognizing the non-self molecules throughout Pattern Recognition Receptors (PRR) which are well evolutionary conserved *"ancient detectors of cellular danger"*. Not only are they present and highly conserved in both plants and animals [9-12], but they are also specialized in which type of non-self-entity could recognize. The Pathogen Associated Molecular Patterns (PAMPs) are specialized to recognize both conserved small molecular motifs - *microbial ligand* - such as lipopolysaccharide LPS (part A of the LPS) or endogenous molecular motifs - *host ligands*-derived from stressed/damaged cells, so called Damage/Danger-Associated Molecular Patterns (DAMPs). Upon their activation by non-self-molecules, they could release small signaling proteins from different cells [13] named cytokines and chemokines. Those molecules can further determine a cascade of tactical defense reactions, culminating with the mobilization of the *antigen presenting cells and leucocytes* at the infection/injured site for pathogens destruction and wound healing. Among the PRRs the most known are the Toll-like receptors (TLRs) that are extensively studied in relation to the body immune response. They are constitutively or induced in almost all types of cells during the course of an infection [10, 14, 15]. When agents such as *pollutants, irritants, pathogens or damaged cells* are sensed by human body, *"a complex biological response of the vascular tissues involving a cascade of biochemical events starts"* leading to what is called acute inflammation. When the acute inflammation cannot eliminate the health hazard

or when the exposure to those agents is repeated, a chronic inflammation could be installed and a long "*simultaneous destruction and healing of the injured tissues"* process is triggered [16-18]. Unfortunately, the immune system could attack its own self molecules under certain pathological conditions. Such process can be encountered in the incomplete clearance of apoptotic cells, when normal mechanism of tolerating self-material is broken and this way starts the on-set of autoimmune diseases.

ONE HEALTH THROUGHOUT POLLUTION MANAGEMENT AND HEALTH HAZARD

"One Health" puts together legislation and research to achieve better public health outcomes. The paper mainly focused on the possible links between pollution, pollution management activities and the propensity of a variety of emerging diseases by answering the question: "How pollution can affect human health?" The necessity to implement "One Health" concept stated in the above-mentioned official documents came from the necessity to mitigate the global pollution environmental impacts on the environment and human health that our society should face.

In this study, the answers to the complex question related to the mechanisms by which pollutants can affect our health were sourced to the increasing evidences citing relevant scientific research results in the field of environment, biology, biochemistry, genetics and medical sciences showing how pollution can dysregulate our defence and adaptation mechanisms. In this paper we focused to specific groups of pollutants like atmospheric less than PM 2.5 particles and also PAH (Poly Aromatic Hydrocarbon), VOC (Volatile Organic Carbon), heavy metals that are usually part of those particles, and their specific influence as well as their role in apparition of a lot of emerging diseases shared among plants, animals and humans. We focussed on those pollutants because they usually are present in the atmosphere and contribute to the climate change and because the aerogenic exposure to such atmospheric pollutants is the most hazardous one when compared to the other pollutants exposure paths such as oral/ingestion or dermal ones. Another reason for why we have chosen those pollutants groups is because they usually result also following the thermal depollution technologies extensively used nowadays to treat both industrial and municipal waste emphasizing this way that even in those depollution activities new pollution issues can arise. With reference to incineration processes except for few almost clean technologies the majority are still generators of large amount of pollutants.

Incineration generates new pollution issues

The atmospheric less than PM 2.5 particles and also PAH (Poly Aromatic Hydrocarbon), VOC (Volatile Organic Carbon), heavy metals are pollutants generated in all kind of industrial process including thermal processing but they are also produced also in industrial and municipal waste incineration. Incineration is known as being among the cheapest processes to reduce large volumes of the generated wastes to be disposed off as result of our anthropic activities as a society including the hazardous ones but they are also the generators of the above-mentioned atmospheric pollutants. It generates also other wastes that should be landfilled. Pollution coming from landfills is complex because it could affect different environmental segments like: air, ground and surface waters and soil. According to their design and construction norms, containers and ecological landfills should be able to limit the direct contact of any municipal or industrial wastes of any type with different environmental segments in order to reduce as much as possible their uncontrolled further environmental transformation under disposal. Unfortunately, that was not the case with older landfills that have been allowed this kind of contact. This way, along the years, the pollution of soil, ground and surface waters and atmosphere have been evolved leading to significant damages to the environment and human health in different areas. Mismanaged wastes represent a recognized source of chemical pollution with hazardous inorganic and organic substances as well as of pathogenic or biological vectors sources comprised of viruses, bacteria, fungus, protozoans, hookworms and insects able to transmit or generate infectious diseases in

plants, animals and humans. Sampling and monitoring pollution related to waste landfills and further fundamental or applied research intended to quantify the pollution risk for the environment and human health have involved a lot of uncertainty due to the complex nature of the pollution phenomena that extends over a large period of time. Although, in last decades, the application of good environmental management practices has been reinforced all over the world by current legislation, but unfortunately it is not enough to achieve significant and durable positive changes for the environment and human health. In this respect, as we have been already mentioned the waste thermal processing is a relevant example. Despite the fact that incineration facilities reduce the volume and hazardousness of both industrial and municipal wastes, their environmental good results are strongly dependent on how the burnt waste have been prior sorted and how incineration facilities are operated and they are generators of new pollution issues. They are recognized as a major source of particulates toxic metals and more than two hundred other organic chemicals generating new pollution issues [19]. Incinerators air pollution abatement equipment catching the pollutants not to be released into the atmosphere only transfers toxic compounds to the fly and bottom ashes. That is precisely why different reports [19] mentioned that landfills with fly and bottom ashes continue to be a source of "persistent air pollutants such as *dioxin, furan and mercury*" that can be dispersed over large regions areas far beyond the incinerators locations, being a real danger for human health.

Pollution landfill effects

Pollutants in general but pollutants' landfills in special can reach our body from our long-life exposure to the substances from the foods and drinking water we ingest and air we breathe. It is a difficult task even for a global collective effort like it is the one proposed under the "One Health" implementation concept to find root causes for many emerging diseases possible linked to the pollution. As a lot of other people working in the environmental fields for some times and being aware about pros. and cons. in evaluating the pollution risk for our health, we have tried to improve in recent years our practical environmental impact and risk assessments approaches by implementing some new multi-criterial decision method. Those methods based on Dempster Shafer theory, Evidential Reasoning algorithm, Rough Set theory, Fuzzy Set theory, Analytical Hierarchy process, etc. have been used in order to reach an environmental sound decision when required, based on expert opinions from different fields [20-30]. The framework of evaluations promoted in those methods involved summing up scientific evidences about pollution effects of different substances at the moment of analysis and presenting them to the professional groups from different fields in order to have an expert, democratic and transparent opinion about possible consequences severity of different presented impacts based on monitoring results. This way we have tried to raise awareness about the link between the assessed pollution sites including landfill pollution sites and health issues of local population presenting them to those professionals that can understand and help to make an environmental sound decision. This way we understood to improve the usual environmental impact and risk assessment approaches *"with the goal of achieving optimal health outcomes recognizing the interconnection between people, animals, plants, and their shared environment"* in the spirit of implementation of "One Health" global concept. In this spirit we can simply improve the environmental impact and risk assessments, when the case, by adding some notes to the monitoring results of example for PM 2.5 particles for which WHO (World Health Organization) has no established safety limits mentioning that: *"ultrafine particulates have the ability to carry pollutants across the blood-brain barrier"* (Oberdorster et al., 2004 cited in [19]). Different studies (Craper et al., 1973; Ehmann et al., 1986; Martin et al., 1989; Multhaup, 1997; Neri and Hewitt, 1991; Pritchard et al., 2004; Rybicki et al., 1993; Thomson et al., 1988, Trapp et al., 1978, Zapatero et al., 1995, cited in [19]) have shown that, *"... substantial increases in neurological diseases (Alzheimer's disease, Parkinson's disease and motor neuron disease) in the last two decades*

(2008, 2012) coupled with earlier onset of those illnesses, were found in almost all developed countries. (...) All those studies found that environmental factors such heavy metal exposure are likely to be responsible for their initiation and progression...".

Someone can argue that the cited literature is old. Yes indeed, but it is relevant for what we all see in relation to the morbidities in nursing homes more recently! We believe that those things mentioned in plain language, easy to be understand by all interested parties involved in a risk evaluation can improve the awareness about such serious health implications. In this way for example we can raise the awareness for those who minimize or ignore the risk due to the atmospheric conditions that can bring sometimes those particles very close to our cities. In this respect it is worth noticing that we cannot stop ourselves breathing and we breath also micronic particles. That is precisely why they might be of greater risk at least for some of us who have some "vulnerabilities" at the corresponding moment and place, i.e. either are children, or are pregnant women or are simply old persons! Such a MCDA (Multi Attribute Decision Analysis) methods for environmental risk assessment for a landfill site for example should be useful in the majority of cases when data to be assessed by evaluators are scarce, incomplete or pervaded by vagueness and imprecision due to fuzzy pollution phenomenon character that nobody is denying [31]. Therefore, the increase of environmental pollution is a fact and human defence mechanisms due to exposure to different pollutants become dysregulated making us vulnerable to all kind of infectious and non-infectious diseases. There is however another fact not to be forgotten! Not only humans are sensitive to pollutants but also pathogens that are forced also to adapt themselves in order to survive. We will extend this debate because pollution with heavy metals can determine changes in the mechanisms the pathogens acquire them in order to survive and that means changes in their genomes and further possibility of emergence of new infectious diseases that plants human and animals can share. *How resilient can we be?*

Health issues

Pollution, including landfill pollution generating significant health issues will be presented next. Any pollutant entering in human body is recognized as non-self-component and triggers the defence mechanisms to neutralize and eliminate it. However, what is not eliminated, it is accumulated generating acute or chronic toxic effects, which could be associated with significant body damages.

Genetic differences between individuals in enzymatic expressions up to 30 %, corroborated with their specific occupations, life style and exposure to different environmental factors could modulate the pollutant clearance process with significant differences from one individual to another. During the lifetime, the human organism is in continuous pollutants contact and attacked via different entering paths such as aerogenic, oral or dermal.

However, from all pollutants' exposure routes, the aerogenic route as we have already mentioned, proved to be the most hazardous because the toxicity of air-borne particulate matters less than 2.5 microns (PM 2.5) released into the atmosphere from different mismanaged pollutants sources including waste landfills. The smaller particles than 2.5 microns are recognized as not being efficiently cleared out by the airways and they can penetrate deeply into lungs, pass into the bloodstream and enter into different cell type where they could produce DNA damages, inducing genotoxicity. In this respect, well documented studies on large cohorts during many years of monitoring records performed in USA demonstrated strong causal associations between municipal waste incinerators locations, their pollutants levels discharges and the increases morbidities in local population such as acute or chronic respiratory infections, asthma, allergies, chronic obstructive pulmonary disease (COPD), life-threatening arrhythmias, exercise-induced ischaemia, thrombotic disease leading to heart failure [19]. It had been also reported 76% increases in mortality from cardiovascular or cerebrovascular disease in postmenopausal women, due to an increase of fine particulates atmospheric pollution concentration up to 10 $\mu g/m^3$. Moreover, mortality from cardiopulmonary disease increased by 37 %, from cancer,

especially lung cancer disease by more than 37%. At the same time, the reports showed an increase of vein thrombosis risk in diabetic patients (DVT - Diabetes Vein Thrombosis) by 70%. Unfortunately, besides the particulates pollution generated by incinerators and their waste landfills, in last two decades, the environment has received increasing amounts of nanometric particles due to the emerging new nanotechnologies and products used in a variety area such as electronics, computers, communications, nanomedicine, agriculture etc. The nanoparticles size (comparable to microorganisms' size) and their possibility to acquire surface charges enhanced their possibility to adhere on many types of surfaces and pollutants, worsening their effect on the environment (air, soil and aquatic systems) [32, 33]. Many scientific groups reported interactions of nanoparticles with biological systems which lead to severe pathological conditions such as chronic inflammatory responses, multifocal granulomas, peribronchial inflammation, progressive interstitial fibrosis, collagen deposition and oxidative stress, all in relation to a dysregulated immune response [32, 33]. That is happening because, as we have already mentioned, when a pollutant cannot be efficiently cleared from the body, it accumulates triggering health damages even at very low concentrations. That is precisely why WHO (World Health Organisation) declared no environmental safety limits for them [19]. For all those hazardous components (e.g. particles less than 2.5 microns, dioxins, furans etc), their discharges into environment should be limited or strictly controlled by appropriate treatment technologies specifically because there are no declared safety environmental limits for them [34]. Finding a cure for a disease even if it is an infectious one, cancer or a neurodegenerative means to find its root cause. The onset and the development of diseases like allergic asthma [35-37], multiple sclerosis, Alzheimer and Parkinson diseases or different forms of cancer [38-40] for example have been intensely studied in last decades in relation to the toxicity of different pollutants and especially in relation to the emitted air-borne particles less than PM 2.5. Next, we will try to offer some more details about them and about how their toxicity manifests by modulating our immunity. PM 25 particles are defined as a complex heterogeneous mixture of solids and liquid particulates. They are usually made of some highly toxic groups of substances such as: PAH, VOC and heavy metals. PAH and dioxin for example represent ligands that can bind to what is known as cellular Aryl hydrocarbon Receptor (AhR). Toxicity of different compounds of chlorinated-p-dioxins is a well-known example to be mediated by this receptor. As chemical nature this receptor is a protein encoded by AhR gene, another very well evolutionary conserved entity. It acts inducing different gene expressions that finally can culminate with DNA damages. It is universally expressed in our cells and it is involved in a variety of physiological processes, including the innate immune response [41-42], and the chemical metabolism of xenobiotics [43]. Relevant scientific proves [44-50] have been brought in the latest years for the link between exposure to the pollution with those respirable particles containing those groups of substances and a plethora of diseases due to the dysregulation of defense mechanisms. The common sense rule points towards the fact that the more a pollutant processing biological entity is expressed in more different body cells the greater are chances that the homeostatic equilibrium to be disturbed somewhere down the road, when body clearance of the processed pollutant or its metabolites cannot be done properly. Immunity is the army that our body strategically evokes and tactically mobilizes each time a hazard threatens its anatomic or functional integrity. Human species has a lot in common with other species including parts of this innate defense mechanism.

So, either are micronic particles that can cross blood brain barrier exposing the brain to toxic pollutants, or are viral infection which in the latest years have been associated to the development of autoimmune diseases like multiple sclerosis, pollution seems to play in important role in the balance of epigenetic genetic factors. So, what we can do in the light of all those presented evidences of increasing pollution due to our economic development on one hand and the increasing number of diseases associated with the exposure to the pollutants on the other? The answer might include but not limited to the following main actions: avoid ecological accidents, reinforce the pollution

environmental impact and risk assessments for all polluted sites determining by all means the involved parties to act responsible, and educate people about pollution and its consequences by citing in those assessment pertinent studies. One of those studies [19] for example that has been focused *"...on a group of middle aged Americans found in their bodies not less than 177 organochloride residues and this is unlikely to underestimate the real number because US-EPA scientists consider that the fatty tissues of the US general population contain over 700 additional contaminants that have not yet been chemically characterized (...) Another recent study made by the Mount Sinai School of medicine measured chemicals in the blood and urine of healthy volunteers and found an average of 52 carcinogens, 62 chemicals toxic to the brain and nervous system and 55 chemicals associated with birth defects..."*.

And in this context, we should educate people that pathogens also as we have already mentioned, adapt themselves in order to survive, suffer mutations and those mutations can increase their virulence and hazard for human health. To add more significance showed by the literature [5, 6] with relevance to the way that bacteria adapt to the environment they inhabit is to mention another relevant example such as *Bdellovibrio bacteriovorus*, a member of the genus of gram negative predatory proteo-bacteria named *Bdellovibrio*. It is a tiny member (0.3 μm up to 1.5 μm) but with a very well-developed genome much higher than someone would expect considering its tiny size, proving this way that is well genetically equipped for its predatory life. *Bdellovibrio* [5] and alike organisms abbreviated as BALO can be found everywhere in the environment from *"soil sample, rhizosphere of plants roots, rivers, oceans, sewage, intestines and feces of birds and animals and even in oyster shells and the gills of crabs"*. It is actually present everywhere. Studying the member of BALO that inhabit fresh water Li et al. [5] found that their ABC system involved in the Fe-S cluster assembly is actually an adaptation for the challenges found in fresh water environment. The same is true for their ABC system for Mn and Zn ions that represents an adaptation for their predatory life being absolute necessary for penetration of cell membranes of other gram-negative bacteria they prey upon and kill. So, their surviving metabolic necessities is linked to the environment where they exist and, in those given examples is linked to the pool of heavy metals such as Fe, Mn and Zn ions existing in this environment transported through the ABC transporting system. Studying those adaptations opens the door for new ways to approach the multidrug resistance for both antibiotics and cancer drugs. Although the things in vivo are much complicated than they look in theory or in vitro, the researchers hope in the future to skillfully use this double edge sword of bacterial adaptation. Harini et al. [6, 34] suggests for example that in the future, using the fact that *Bdellovibrio bacterivorous* species manifests resistance to beta-lactam antibiotics might transform it into a natural controlling agent because it is well adapted to its predatory life and it is able to kill other pathogenic agents even in a beta-lactam antibiotics environment. This approach might be helpful to treat periodontitis cross infections recognized as a high inductor risk factor for osteoporosis and pulmonary infections.

Pollutants

In this section we will take a closer look to the heavy metals pollution because besides PAH (Poly Aromatic Hydrocarbon), VOC (Volatile Organic Carbon) they are major components of the micronic airborne particles. They form actually the solid part of the airborne particulate matters coming from different pollution sources including mismanaged waste landfills. In the atmosphere they can encounter other particulates matters being subject to all kind of redox reactions in solid or droplets liquid phases. Heavy metals from mismanaged waste can be found also in other environmental segments such as soil, ground waters and surface waters coming from landfills` leachates. Next, we will briefly try to present why heavy metals represent a very special type of pollutants. Here are some facts: they are part of usual environmental background, they cannot be destroyed, they just transform in the environment changing their oxidation state. Their evolution in environment is very complex. Their residence time as well as their transformations depend both on specific properties of metals and the properties of the local environment segments such as humidity, pH, redox potential, etc. where they exist. All

these factors can influence metal bio accessibility/bioavailability as well as their, bioaccumulation/bioconcentration and finally their environmental toxicity for different species that absorb them for their metabolic necessities. Because each species from viruses and bacteria to superior organisms has its own metabolic necessities it is a real issue to define PBT critical levels (acronym for Persistent, Biocumulative and Toxic) to evaluate their ecotoxicity [45, 46]. Due to the fact that they are an integral part of biological proteins their essentiality in order to sustain the existence of each species is different, and so it is the level of toxicity for each species. World-wide statistical data report that a lot of infectious diseases are associated with endemic areas where population manifest a high rate of deficiencies in essential trace metals. However, it is equally true that there are also other statistical data that report a high prevalence of those infectious diseases in highly industrialized countries, associating them with the exposure of the local population to high heavy metal loads from atmospheric industrial emissions. Facing those apparently contradictory facts and analysing the link between pollution with heavy metals and different infectious diseases, scientists [47] concluded that *"the combined effects of exposure to metals and pathogens on the burden of disease in human populations remain unknown, but there is no doubt they are being modified by the increasing contamination of the environment with metals"*. To enter cellular metabolism heavy metals should be under ionic form and in different biological settings this process is done by association with other molecular entities or compounds. Those entities or compounds function as ligands that contain N, O, S with electronic availabilities to bind metals. We have only a finite number of heavy metals but practical infinite number of electronic interactions from different entities functioning as metal ligands depending on local conditions. As part of bacterial and viral proteins, heavy metals play an important role in their survival and pathogenesis. The most common metal ions found in viral proteins are for example zinc, magnesium and copper. The deficiency of those trace metals can alter the viruses` genomes leading to the emergence of new infections [47]. The implications of how the metals can be acquired by different species in a depleted or enriched cellular environment is of paramount importance because humans are living together with the so called good bacteria and dormant viruses and when we acquire an infectious disease our body become a biochemical battle field where all those species are trying to gain tactical surviving advantages. We mentioned that ABC transporters gene family is one of the possible oldest very well evolutionary conserved entity. ABC transporters in bacteria can be responsible for their virulence even if, in the non-pathogenic bacteria that inhabit our gut for example, the ABC genes are less well represented than in pathogenic ones. However, when local conditions might be favourable different invading pathogens, in close proximity to each other's in our body, can make some horizontal gene transfer making their own surviving pact with other locally found neighbouring bacteria (see horizontal gene transfer in oral cavity). This way they become adapted to the local conditions in order to survive and not in our advantages. Recent studies have reported possible microbial driver in neuroinflammatory diseases like Alzheimer and Parkinson by *Porphyromonas gingivalis*. This is a bacterium present almost always in subgingival plaque in periodontitis. Recent studies reported that it can be linked to the clinical pathological conditions like systemic inflammation, hypercoagulation, presence of amyloid fibrin (ogen) in plasma as well as structural changes in platelets, manifest in Parkinson disease patients [48, 49]. Metal biochemistry in living organisms is governed especially by coordinative chemistry that allows the flexibility to realise local bonds depending on the cell necessities, assuring the extraordinary dynamics required by the energetic biochemical reactions. That means that although affinity for one metal ion, for example Zn ion, might be higher than for another one for example Fe ion, it is actually the metal speciation that will prevail by favouring the binding of Fe ions. As the literature mentions [45, 47, 50] in those cases *"alternative selection of metal could occur at kinetic level by using a special metal shuttle (metallochaperones), that are able to overcome the thermodynamic constraints"* lowering the energetic barrier of the transport process [47, 48, 50, 51]. Understanding this mechanism, we understand

that polluting the environment with heavy metal can break the local environmental balance and reshape the local distribution of viruses and bacteria populations increasing the incidence of some diseases. In this respect for example

".....the World Health Organization (WHO) and the Food and Agricultural Administration (FAA) suggest that the population mean intake of Cu should not exceed 10-12 mg per day for adults because: the deficiency of Cu in the human body would increase the risk associated with developing coronary heart disease, while the Menke's disease, Alzheimer's disease, Parkinson's disease, Wilson's disease, and Occipital Horn Syndrome are implicated with the excessive amount of Cu uptake and excretion...." [52].

We know that in science any hypothesis should be sustained by proves. Tracking a link between pollution with toxic heavy metals and different diseases either infectious or non-infectious means bringing proves by measurements about the mechanisms those metals are metabolized in certain way in different tissues, in different species including humans. Determination of metals form within different complexes in vivo remains the main challenge. However, the monitoring science progresses and using for example X-ray fluorescence microscopy (XRM–X-Ray Microscopy) imaging (Fahrni, 2007 in [47]) can help us to measure metal identity and amounts [47, 48, 52] at different cellular and even subcellular (organelles) levels.

Another way to prove different type of metal implications in the development of different infectious and non-infectious diseases is to use some proteins sensitive to the modification of cellular normal physiological concentrations, as markers of possible pathological conditions.

The so-called heat shock proteins, denominated with the abbreviation HSP followed by a number representing their molecular weight, are cellular entities involved in assisting other proteins in folding and maturating in the cell. They have also important signalling functions of changing homeostatic physiological parameters like: temperature, pH, level of water, oxygen or nitrogen, heavy metals etc. Because the genes encoding those proteins were found to be over expressed in abnormal physiological conditions, those proteins become interesting entities to be studied as markers/sensors for cellular and environmental stress conditions both in prokaryotes and eukaryotes organisms. Their investigation is especially linked to pathological conditions such as inflammation, infections and cancer. In this respect HSP 70 and HSP 90 are the most studied proteins for their link to the mutant and normal expression of another entity named p53 protein - known as tumour suppressor protein - that regulates cell apoptosis. In cancer studies, there are two main approach for research namely to studies the onco-entities and those that suppress the onco-genesis such is the p53 protein. We also should mention that latest research has reported that gene encoding HSP 70 protein was found also to be over expressed in plants stressed with Cd, As, Hg considered also toxic heavy metals for humans. Consequently, new possibilities are open in relation with HSP 70 protein in order as an indicator of environmental heavy metal stress [53-55]. Cadmium toxicity in humans for example is hypothesized to be linked to different hormonal signalling pathways being considered an endocrine disruptor. Its toxicity derives from the fact that it can bind to oestrogen receptor alpha even in very low doses. Its interference affects signal transduction along the oestrogen and MAPK (Mitogen – Activated Protein Kinase) signalling pathways, the latest one protein kinase being involved in directing cellular response to a large number of stimuli such as mitogens, osmotic stress, heat shock proteins, proinflammatory cytokines, UV radiation, etc. This way it regulates cell functions such as: gene expression, cell mitosis, cell differention, proliferation, survival and apoptosis. As environmental pollutants Cd can be easily found in waste battery, as component of semiconductors parts. Due to its toxicity in very low doses it can also be used in molecular biology research as to block voltage dependent calcium channels from fluxing calcium ions, as well as in hypoxia research to stimulate proteasome-dependent degradation of Hif - 1 α (Hypoxia-inducible factor), transcription factors that respond to decreases in available oxygen in the cellular environment. Cd is under preliminary research for its toxicity in humans, potentially affecting mechanisms and risks of cancer, cardiovascular disease, and osteoporosis [56]. Environmental sensors for heavy metal pollutants are much needed because we can be exposed to them also by ingested food via contaminated water or contaminated crops and

vegetables. For humans some of the heavy metals` ions are considered essential to name for example Fe^{3+}, Fe^{2+}, Cu^{+}, Cu^{2+}, Zn^{2+}, others are called non-essentials and they are toxic (Al, As, Pb, Hg, Cd, etc.). Abnormalities in the normal homeostatic mechanisms of the body can lead to temporary or permanent dysfunctionalities. Those dysfunctionalities are linked to the decreased concentrations - insufficient metals in organism - to realize the normal metabolic functions or to the increased concentrations due to their accumulation and inadequate elimination possibilities that make them available in the context of different local specific tissue/cellular/subcellular reactions mechanisms where they can generate ROS (Reactive/Radical Oxygen Species) responsible for cellular membrane damages. We know that reactive oxygen species are the cause of cellular damage. Those non-essential metals for human bodies can determine increase of the radicals in our body as they accumulate and also can make bacteria or fungi to improve their surviving strive in our body. Some very common diseases such as diabetes type II non-genetic insulin resistance, obesity or Coronary Artery Disease (CAD) [57] started to be linked to the potential of ROS generation in organism by the toxic heavy metals.

In latest years, we have joined the global effort to achieve optimal health outcomes focusing our research interests on a variety of topics such as: environmental impact and risk assessments and waste hazardousness [58-65] or environmental pollution monitoring [66-68] in the spirit of implementation of one health concept helping to acquire useful data in order to sustain future endeavors.

CONCLUSIONS

If we will continue to recognize the signs of profound changes we going through due to the pollution, but we will not have a harmonized targeted system of actions to protect human health and environment-the only home that humankind has-future generation will pay the consequences of our long-term ignorance.

How innate immunity guards our body and how acquired immunity is supported and communicates with the innate immunity once pollutants enter our body is still a topic of debate. Because the interactions might be so dependent of species and individual particularities, a rhetoric question arises *"can we ignore the existing evidences that show that a plethora of century diseases might be linked to the pollution?"* Of course, we cannot. It is too risky to ignore them and, even if we would be tempted to do so, the way that latest epidemic and pandemic diseases evolved are forcing us to reconsider our attitude.

We have tried to present only some of the most recognized evidences of the pollution and the way pollution might affect our health by introducing some very specific concepts that immunologists are working with in an attempt to signal the high implications that might exists when ecological equilibrium might be disrupted.

In the spirit of the implementation of "One Health" concept, scientific evidences of high quality should be brought always by professionals of our society and based on them appropriate measures should be taken in order to defend the health of our society as a whole and of each individual in part.

In order to attend those desiderates education in the environmental protection should be reinforced with new innovative way to explain people the importance of the topic in order to raise awareness about the hazards brought by pollutants. Explaining the pollution risk in simple terms we should be able to mitigate those risks by making people aware about their own vulnerabilities in the face of those hazards. This way we will be able to mitigate those risks up to a level recognized as ALARA i.e. As Low As Reasonably Achievable.

ACKNOWLEDGEMENTS

These researches were performed by National Research and Development Institute for Industrial Ecology with the financial support of the Romanian Research and Innovation Ministry – PNCDI III, Program no.1 - Development of the national research-development system, Contract 002 PFE / 16.10.2018.

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