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Extremely Polluted Environment Reflected in Degenerative CNS Diseases

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Abstract

We followed up the effects of environmental contaminants on possible induction of central nervous system damage. Our attention was focused on the effects of nanoparticles and microparticles and their role in development of multiple sclerosis and other neurodegenerative diseases of the central nervous system in regions of Czech Republic with known extremely polluted environment and historically high prevalence of these diseases. We also followed the role of nutrition, which not only plays a role in the development of these diseases but can also be used medically. Vitamin D and beta glucan supplementation is discussed, particularly their use in possible regulation of immunopathological processes.

Keywords: Noncommunicable diseases; CNS; Nutrition; Vitamin D; Beta glucan

Abbreviations

ADP: Amyloid Precursor; CNS: Central Nervous System; EBV: Epstein-Barr Virus; WAT: White Adipose Tissue

Introduction

Relations between human activities and the surrounding environment have lately become highly important topics. Environmental pollution and its effects on human health is increasingly revealed with the help of new technologies, allowing for better definition of harmful materials causing pathophysiological processes and resulting in numerous diseases [1,2]. Human activities often have negative effects on water, air, and soil conditions. Negative effects of urbanization and industrialization, so called anthropogenic pollution, seem to be the biggest risk for deterioration of human health. This damage can start during pregnancy, continuing through childhood and into adulthood [3,4]. The final level of damage is a summary of voluntary and involuntary exposition to damaging agents and reflects the risk of noncommunicative diseases [5,6]. Total prevalence of these diseases is based on genetic, epigenetic, nutritious, climatic, geographic, and socioeconomic factors [6]. Among numerous organs susceptible to this impact is the cardiovascular system, respiratory system, function of the skin, and urogenital and gastrointestinal systems. Significant attention has focused on possible damage impacting the Central Nervous System (CNS) [1,3,6-8]. Developmental immunotoxicity together with perinatal programming of the individual suggests the possibility of CNS damage occurring at an older age [5,7]. Immunopathologic events accompanying and affecting these diseases are being evaluated [4,9]. Intensity and length of exposition influences the development of tumors, diseases of cardiovascular system, respiratory problems, allergy, urogenital tract problems, osteoporosis and osteoarthritis, diabetes, autoimmune diseases, cataracts, and diseases of CNS-most of all Parkinson disease, Alzheimer disease, and multiple sclerosis. Environmental pollution is the prevalent pro-inflammatory stimulus for CNS with subsequent induction of development of neurodevelopmental disorders [1,3-5]. Particles of PM0.1 size can be found in the CNS within 4-24 hr after inhalation. When inhaled nasally, they enter the CNS 7 days after exposition [2]. A correlation between low-quality environment and prevalence of multiple sclerosis in the Czech Republic has been reported [10]. With the better understanding of new contaminants, the extent of the spectrum of diseases affected by high exposure to environmental contaminants may become more apparent [1,3,5]. Nanoparticles and microparticles seem to be the most important components penetrating the CNS not only through the blood stream in the respiratory tract, but also directly through nasal inhalation via nervus trigeminus [1,2].

The Usti region is one of the most contaminated regions in Europe. With an area of 339km^2 and 821,000 people, it is a center of industry and energy in the Czech Republic. Usti's chemical industry specializes in the manufacturing of diesel fuel, heating oil, and fertilizers, and the glass industry represents more than 170 large companies. Surface brown coal mining represents more than 60% of the entire energy needs of the country. In this region, we can find five coal power stations producing more than 25,000 GWh annually.

The main component of pollution released by mining and processing of coal consists of particles smaller than PM1 [11]. Extreme environmental pollution occurs during winter, resulting in a high prevalence of diseases, particularly among children. In addition, a high frequency of noninfective diseases is common, leading to a significantly lower lifespan of the local population (approximately 3 years shorter lifespan). The major problem represents particles released during mining, transportation and processing of low-quality brown coal, with the common size ranging from 20 to 1000 nm [11].

In addition, the complex of environmental pollution harmful to humans and other species includes various chemical mixtures and biological materials contaminating the air. Pollution can be artificial (i.e., industrial) or natural (i.e., volcanic eruptions) [5,11]. According to a regulatory agency, the effects of contaminated environment is responsible for the early death of more than 3 million people.

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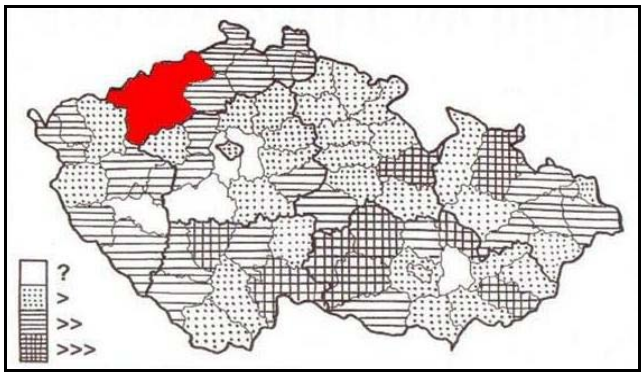

Figure 1: Occurrence of multiple sclerosis in individual regions of the Czech Republic. (?): Not known; (>): Low frequency; (>>): Prevalence higher than 125/100,000; (>>>): Prevalence higher than 150/100,00; and Red: More than 160/100,000 (based on [10]).

These deaths are connected to a higher frequency of cardiovascular diseases, cancer, allergies, and other noncommunicable diseases. Recent studies have suggested that these contaminants might have both direct and indirect effects on induction of diseases of the CNS including Parkinson disease, Alzheimer disease, and multiple sclerosis. The induction of neurodegenerative processes occurs in early age, particularly in individuals persistently exposed to the high levels of contaminants mentioned above [1,4,7]. The mechanism leading to the damage of CNS is still not fully understood, but the role of undefined nanoparticles and microparticles, oxidative stress, activation of immune processes involving inflammasomes, and some genetic and epigenetic influences are clear [12,13]. The high frequency of multiple sclerosis in the Usti region (Figure 1) first reported over 30 years ago [10] and the increasing prevalence since were the inspiration for this short review.

The role of environment on the function of CNS is being intensively studied and, with the help of technical development, we can define individual contaminants in full details. It is important to note, however, that many authors have suggested possible neurotoxic effects of these harmful substances even before we could adequately describe them. Our group published a comparison of prevalence of various diseases among different regions of the Czech Republic in 1993 [9]. In all three children age groups (i.e., >5, 5-14 and <14 years of age), we found that the occurrence of allergic diseases is elevated 170%, mental problems 166%, respiratory diseases 234-250%, and diseases related to social-economic conditions 152-570% [9]. A realistic view confirming our findings can be found in the pioneering work of Calderon-Garciduenas, which defined effects of immunotoxicity on dysregulation of the immune system accompanied by systemic inflammation in children [4]. A detailed study of the clinical manifestation of CNS disease related to the effects of toxic substances present in the environment and to the mechanisms of the transfer of microparticles strongly suggests further research is warranted [5], particularly in relation to autoimmune diseases [14].

New findings of developmental immunotoxicity and perinatal programming with epigenetic alterations showed that at an older age, it can result in a wide scale of clinical problems [7]. An excellent study evaluating the quality of the environment in the Usti region and in the neighboring region in Germany, which is divided by mountains Krusne hory, clearly confirmed the risks of a polluted environment [15]. In these two closely neighboring regions, these is a clear correlation between the level of pollution and the overall health of the entire population.

Multiple sclerosis is a chronic multifactorial disease of the CNS characterized by demyelization, inflammation, and neurodegeneration. Major inductors of this disease are considered genetic factors and effects of environmental conditions, smoking, nutrition (particularly low vitamin D level) and EBV infection [16-18]. Currently, there is no doubt that a low vitamin D level is associated with a higher risk of multiple sclerosis [19], but the full impact of vitamin D supplementation is still not clear [16-18,20]. In addition, a strong association of multiple sclerosis with HLA genotype HLA-DR B1 was suggested. Vitamin D influences anti-inflammatory immune response and elevated levels of T regulatory lymphocytes with simultaneous depression of the level of pro-inflammatory helper cells Th1 and Th17. High-dose supplementation results in reduction of the level of EBV antinuclear protein (ENNA 1) and overlap of EBNA2 with VDR, suggesting a genetic effect in interaction between genetic and environmental risk factors for multiple sclerosis [16]. In the last 30 years, we can observe a steady increase in the prevalence of multiple sclerosis worldwide. In the Czech Republic alone, the increase represents at least 30% [21]. The actual occurrence of multiple sclerosis fully corresponds to the full definition of the disease, which is possible due to new multidisciplinary approaches to diagnosis the disease [22].

Alzheimer disease can be specified as a multifactorial metabolic disease, characterized by depression of multiple cellular functions. The most common is alteration of proteolytic processing of Amyloid Precursor (ADP), resulting in formation of neurotoxic amyloid beta plaques, phosphorylation of Tau protein, and problems with the metabolism of lipids and energy [16]. Some studies assumed the role of herpetic diseases (e.g., HSV1, HHV 6A and HHV 6N) on induction of production of beta amyloid, possibly with significant involvement of IgG_3 [23]. These effects result in persisting inflammatory reaction, which can be directly induced (among other effects) by microparticles present in our environment. In addition, the pathophysiological manifestation is affected by the low levels of vitamin D. Several detailed studies clearly found that vitamin D deficiency is a strong risk factor for both Alzheimer disease and dementia. Adequate supplementation with vitamin D can significantly improve clinical manifestation. In addition, glucan supplementation has had positive effects [24].

Parkinson disease is characterized by the presence of dopamine-producing neurons in substantia nigra, typical Lewi bodies, and synuclein aggregates [5,16]. Significant vitamin D deficiency is also a characteristic of this disease, which has positive effects on dopamine synthesis in CNS via protection against dopaminergic toxins. Vitamin D supplementation results in reduction of zinc-caused oxidative stress in substantia nigra [16], leading to the hypothesis that low levels of circulating vitamin D result in dysfunction or even death of cells within the substantia nigra [25].

Studies of the etiological role of obesity inducing autoimmune diseases result in new, significant findings defining not only food predisposed to induction of autoimmune diseases, but also food and

its components, which suppress the risk of these diseases [26]. A developed society whose diet does not correspond to an intake and expenditure of energy (so called Western diet) suffers not only with high risk of obesity, but also with a steady increase of occurrence of autoimmune diseases [14,26,27]. Obesity is a major risk factor for noncommunicable diseases. In many countries, the association between obesity and noncommunicable diseases is higher than 30% [27]. Obesity can be defined as excessive accumulation of fat, which, together with metabolic syndrome and low-level systemic inflammation negatively regulates our health [18,28]. Accumulation of White Adipose Tissue (WAT) is considered to be an endocrine tissue [8,14], producing various pro-inflammatory mediators, such as TNF-α, IL-6, leptin, CRP, and others, which subsequently start chronic low-grade inflammation [27]. The abovementioned signals of fat cells affect some subpopulations of T lymphocytes particularly Tregs and Th17. Leptin not only regulates energetic balance, but also stimulates proliferation of Th1 cells via its binding to leptin receptors present on some T lymphocytes. Current nutrition also results in dysmicrobia of the gastrointestinal tract and in changes of microbiome with subsequent changes of the secretory immune system and possible induction of autoimmune diseases. Adipokines and lipokines produce autotaxine, affecting neurogenesis, which might play role in neurodegeneration [8]. Fat cells are in contact with naive T lymphocytes, which can participate in undesirable signals between adaptive and innate branches of the immune system resulting in T cell-mediated reaction to persisting inflammatory impulses [18]. Based on this information, we need to focus our attention on nutritional changes, particularly in view of possible blocking of negative effects of toxic substances present in our environment [26]. Fundamentally, a high-quality environment is required, achieved through gradual reduction of the harmful material. We believe that food supplements, specifically, nutritional supplements, which can substantially influence effects of persisting inflammation, offer an opportunity to regulate the occurrence of diseases mentioned above. A good choice would be documented supplements able to prophylactically reduce the effects of some dangerous components (such as supplements with anti-oxidative effects) and show a positive role in amelioration of some diseases [29-31]. As the damage of CNS can occur at an early age, it is important to not only eliminate well-defined harmful substances, but also to support immune mechanisms damaged by persistent environmental pressures [2].

Approximately 90% of seniors in Western countries are vitamin D deficient [16]. We reviewed records of our Immunological Department over a 10-year period and found vitamin D deficiency in patients from 85% in summer (May to October) to 95% in winter. We found the level of vitamin D below 15ng/ml in 35% of individuals. In agreement with findings from numerous other countries, we see a pandemic deficiency of vitamin D in the Western population, which results in numerous clinical problems. Correlation of the low level of vitamin D with the higher risk of cancers, autoimmune diseases, and infectious diseases is already well established. Epidemiologic and clinical studies have clearly found a connection between low vitamin D levels and higher risk of neurovegetative diseases [16]. Based on these findings, we believe that it is important to focus on these problems and evaluate the effects of vitamin D on formation and development of these diseases. In addition, for multiple sclerosis cases, we can even consider vitamin D as a direct medication [32]. A genetically reduced level of 25OHD is significantly correlated with increased risk of multiple sclerosis development [17]. Vitamin D has a positive role in synthesis and accumulation of dopamine and, at least in experimental conditions, regulates prevention of oxidative stress. Several pathophysiological manifestations of CNS connected with oxidative stress have been described and can be influenced be prevention. Beta glucan can play an important role in these processes not only as a supplement, but also as a part of nutrition [33]. The ability of beta glucan to regulate levels of various lipids, including cholesterol, apolipoproteins, triglycerides, and leptin, has a direct effect not only in prevention, but also in treatment of these diseases [29-31,33,34]. In our laboratory, we repeatedly described reparation of damaged parts of nonspecific and secretory immunity by beta glucan supplementation of children [31]. Positive modulation of the nonspecific branch of the immune system by application of beta glucan results in increased immunosurveillance. Some studies suggested that beta glucan supplementation leads to increased resistance to the toxic substances [33,35]. Beta glucan has been recently shown to have antidepressant effects, which are manifested via enhancing the prefrontal Dectin-1/AMPA receptor signaling pathway [36], opening a new window for the use of beta glucan. Another study found protective effects of beta glucan in brain tissue, acting via its significant antioxidant activity [37]. The possibility of direct effects of beta glucan on brain cells cannot be overlooked, as glucan receptors were found on microglial cells [38]. This hypothesis was further supported by findings that glucan supplementation increased the number of brain cells in the substantia nigra of animals with Parkinson disease [39], leading to the patent for use of beta glucan in treatment of multiple sclerosis [40].

These data show positive effects of nutrition on modulation of damaging effects of environmental pollution. We conclude that the use of well-studied and well-defined supplements, such as beta glucan, is a significance step leading to amelioration of risks of development of chronic health problems of Western civilization [26,33].

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