Are the civilization diseases the result of organohalogen environmental pollution?

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The notion of ‘civilization diseases’ is used to describe certain ailments whose aetiology is difficult to explain based on the knowledge about the functioning of the body and its metabolism. Only studies at the cellular level, on biochemical changes shed light on the causes of some diseases described as civilization diseases (cancers, cardiovascular and respiratory diseases, obesity, psychomotor disorders in children and an increase in the frequency of malformations). The factors whose incontestable influence on the increase in the frequency of occurrence of various ‘civilization diseases’ has been proved are persistent organic pollutants, among others belonging to the group of organohalogen compounds. Among organohalogen pollutants one needs to distinguish organochlorine compounds, which have been used as pesticides, and pollution emitted by various industries such as dioxins andfurans, polychlorinated biphenyls, and polybrominated organic compounds used as flame retardants and perfluorooalkylated substances, which are characterized by high chemical and thermal stability as well as high surface activity due to which they may be widely used as oleophobic and hydrophobic factors.

Key words: POPs, PCBs, PBDEs, dioxin, PFASs, civilization diseases

INTRODUCTION

The notion of ‘civilization diseases’ is used to describe certain ailments whose aetiology is difficult to explain based on knowledge about the functioning of the body and its metabolism. Only studies at the cellular level, on biochemical changes shed light on the causes of some diseases described as civilization diseases (cancers, cardiovascular and respiratory diseases, obesity, psychomotor disorders in children and an increase in the frequency of malformations or neurodegenerative diseases). For example, in recent years mental and behavioural disorders have increased by more than 37% (Parkinson’s disease increased by 75%, Alzheimer’s disease doubled, autism increased by 30% and attention deficit hyperactivity disorder (ADHD) increased by 16%) (WHO, 2012a; Zeliger, 2013).

The factors whose incontestable influence on the increase in the frequency of occurrence of various ‘civilization diseases’ has been proved by numerous studies are persistent organic pollutants (POPs), among others belonging to the group of organohalogen compounds. They have been the subject of increasing anxiety for many years, especially in the context of possible biological exposure, including internal exposure coming from releasing compounds collected in an organism. All those compounds the World Health Organization (WHO) has classified as endocrine disruptors (EDs), which are the substances affecting the hormonal balance of an organism (WHO, 2012a).

Among organohalogen POPs one needs to distinguish organochlorine compounds, which have been used as pesticides (OCs), and pollution emitted by various industries such as dioxins (PCDDs) and furans (PCDFs), polychlorinated biphenyls (PCBs), and polybrominated organic compounds used as flame retardants (FRs) and perfluorooalkylated substances (PFASs), which are characterized by high chemical and thermal stability as well as high surface activity due to which they may be widely used as oleophobic and hydrophobic factors.

Numerous research showed that food, especially of animal origin, including fish and seafood, is the main source of exposure for the human organism (Darnerud et al., 2006; Domingo, 2004; Frederiksen et al., 2009). Table 1 presents POPs content in selected food products. For infants and young children, the group most sensitive to these xenobiotics, an important source is breast milk (Table 2), as
well as domestic dust which is an additional source of exposure to these compounds.

Biological monitoring of those compounds in human fat tissues provides information on the amounts accumulated by the individual from all the sources through their life and, potentially, what concentrations they may be exposed to in case of their release, e.g. while being on a diet or during lactation. It is commonly known that lactation, which may be considered as involuntary cleaning of the female organism is one of the most common ways of releasing the organohalogen compounds (Czaja et al., 2006; Covaci et al., 2008; Crisp et al., 1998; Fernandez et al., 2008; Hernik et al., 2014; Knutsen et al., 2011, Pulkrabova et al., 2009). Both phenomena provide information about the exposure in the past whereas the information about the size of the current exposure form external and internal (endogenous) sources may be obtained from the tests of those compounds' levels in the serum of peripheral blood or in umbilical cord blood in case of prenatal exposure (Axmon & Rignell-Hydbom, 2006; Gari & Grimalt, 2013; Ingelido et al., 2009; Kirman et al., 2011).

The biomonitoring of compounds adversely affecting human health is an indispensable tool for the assessment of threats resulting from environmental pollution while providing substantive grounds for risk management (Table 3).

The monitoring of trends of those compounds levels in various environmental elements including the human being is particularly crucial when they are banned from
use due to their toxicological properties. It applies to e.g. POPs which belong to organohalogen compounds, which have been banned (OCs for over 40 years, PCBs for 20 years, PFASs for 5 years), and, nonetheless, they are still present in the environmental samples.

Systematic knowledge about the tissue deposit levels of selected organohalogen compounds, their sources and human exposure to these compounds in comparison to the occurrence of civilization diseases can be an important tool in public health management. Therefore, the aim of the work was to review and systematize the information on the impact of the selected persistent organic pollutants on the occurrence of civilization diseases.

**CHARACTERISTICS AND THE EFFECTS OF CHOSEN ENVIRONMENTAL POLLUTANTS**

Historically, the first chloroorganic compounds that due to their toxicological properties were subjected to restrictions of the Stockholm Convention were organochlorine pesticides (OCs) such as DDT and its metabolites or Lindane, which were widely used in crop protection, sanitary hygiene and as veterinary drugs. **Dichlorodiphenyltrichloroethane** (DDT) is degraded to DDE (1,1-dichloro-2,2-bis-(p-chlorophenyl)-ethylene), which is the most persistent DDT metabolite. DDE (in the form of the p,p′-DDE isomer) in the environmental samples, including the human body, occurs at the highest concentrations. In the case of DDT, as a representative of the entire OCs group, numerous studies have shown its role as a precursor of carcinogenic processes in humans (breast cancer, leukaemia, lymphomas), as well as its significant contribution to the formation of endometriosis, ovarian dysfunction, lower testosterone levels and the risk of obesity in children exposed during the perinatal period (Czaja et al., 2006; Góralczyk et al., 2015; Kirman et al., 2011). It should be mentioned that the research results have also indicated the role of organochlorine pesticides in the development of Parkinson’s disease and Alzheimer’s disease (WHO, 2012a; Zeliger, 2013).

**Polychlorinated biphenyls (PCBs)** is a group of chemicals with various numbers of hydrogen atoms substituted by chlorine atoms in both benzene rings. 209 potential PCB congeners with different toxicological properties have been identified. Some PCB congeners exhibit similar toxic effects as the so-called dioxins – dioxin-like PCBs (DL-PCBs). This group of PCBs has also been included in the concept of toxicity equivalents (TEQ) when estimating the health risk when exposed to this group of compounds. PCBs are very persistent in the environment and transported over long distances by air and water currents in accordance with the concept of grasshopper which leads to global environmental pollution with this group of compounds. Numerous studies have shown the evident effect of these pollutants on the development of endometriosis, uterine fibroids, as well as thyroid and adrenal glands disorders, and reduced psychomotor and cognitive development in children. These compounds are also suspected of potentially increasing the risk of developing prostate and breast cancer as well as dysfunction of the immune system and may be the risk factors for Parkinson’s disease (EFSA, 2010; Hoyer et al., 2014; Hoyer et al., 2015; Meijer et al., 2008; WHO, 2012a; Zeliger, 2013, Zheng et al., 2017).

**Dioxin** is a term used to describe a family of substances including polychlorinated dibenzo-p-dioxins (PCDD), polychlorinated dibenzofurans (PCDFs) and dioxin-like PCBs (DL-PCBs). Among 75 PCDDs, 135 PCDFs and 209 PCBs, respectively 7 PCDDs, 10 PCDFs and 12 DL-PCB congeners are characterized by high toxicity to humans. These compounds have a similar structure and are characterized by a common biochemical mechanism of action and similar toxicological properties.

### Table 3. Levels of selected POPs in the biological material from different countries

| Country | CB-153 | ΣPCBs | ΣDL-PCBs | BDE-47 | BDE-153 | BDE-209 | ΣPBDEs | OCs | PFOA | PFOS | ΣPFASs | Ref. |
|---------|--------|-------|---------|--------|---------|---------|--------|-----|------|------|--------|------|
| **Fat tissue [ng x g⁻¹ fat]** | | | | | | | | | | | | |
| France | 58.90  | 137.06 | 4.46    | 0.32   | 1.12    | N.D.    | 1.59   | –   | –    | –    | –      | –    |
| China  | 5.80   | 13.50  | 0.31    | 2.47   | N.D.    | 3.05    | –      | –   | –    | –    | –      | Ploteau, 2016 |
| USA    | 39.10  | 92.70  | N.D.    | N.D.   | N.D.    | N.D.    | –      | –   | –    | –    | –      | Ly, 2015 |
| **Blood/serum [μg x L⁻¹]** | | | | | | | | | | | | |
| France | 113.30 | 281.35 | 0.18    | 0.48   | N.D.    | 0.75    | 33.20/118.00 | 5.07 | 24.08 | ND   | –      | Ploteau, 2016, EFSA, 2015 |
| Poland | 43.40  | 57.05  | 0.67    | 1.00   | 0.40    | ND      | 1.40   | ND/506.30 | 2.83 | 8.42  | 14.70 | –      | Hemik, 2015, Góralczyk, 2015a, Góralczyk, 2015b |
| USA    | 19.80  | 59.21  | N.D.    | 20.50  | 5.69    | <LOD    | 31.31  | <LOD/238.00 | 3.07 | 9.32  | 15.59 | –      | EFSA, 2015 |
| China  | ND     | ND     | 0.97    | 2.64   | N.D.    | 3.97    | –      | –   | –    | –    | –      | Ly, 2015 |

All results are given as a median. ΣPCBs, six indicator of PCBs (CB-28, CB-52, CB-101, CB-138, CB-153, CB-180); ΣDL-PCBs, dioxin-like PCBs (CB-77, CB-81, CB-126, CB-169); ΣPBDEs, sum of BDE-28, BDE-47, BDE-100, BDE-153, BDE-209), BDE-47, congener from PBDEs group treated as a biomarker of exposure to the whole group of PBDEs and occurs at the highest concentrations in the biological material, and BDE-209, congener from PBDEs group treated as a biomarker of exposure and occurs at the highest concentrations in house dust. ΣPFASs, sum of PFHxS, PFOS, PFOA, PFNA, PFDA, PFUnDA, PFDoDA, PFOA and PFOS, representatives of the whole group of PFASs, which occur in the highest concentrations in environmental samples, food and biological material. N.D., not determined and no data, LOD, limit of determination.
As demonstrated in numerous studies, exposure to this group of compounds in early childhood or in the prenatal period may in adulthood result in a decrease in the semen quality and increased risk of testicles cancer, as well as a gender imbalance with fewer male offspring. For these xenoestrogens, an increased risk of breast cancer and endometriosis and the prevalence of menopause at an earlier age has also been demonstrated (Darnerud et al., 2006; Struciński et al., 2013; WHO, 2012a).

Polybrominated diphenyl ethers (PBDEs) are a mixture of diphenyl esters with a different number of hydrogen atoms substituted by bromine. Because of the different substitution site and the different number of bromine atoms, there are 209 possible congeners with different toxicological properties. Like PCBs, they are transported over long distances with air and water currents. Some PBDEs are subjected to bioaccumulation and biomagnification in the food chain, and they are present in biological materials, including human tissues, excrements and excretions. Their presence in the human body has a proven adverse effect on the occurrence of certain diseases, e.g. early maturation, cryptorchidism, as well as a significant effect on the secretion of thyroid glands and cognitive disorders in developing organisms and diseases of the nervous system such as autism and ADHD (Chevier et al., 2010; Costa & Giordano, 2007; EFSA, 2011; Meijer et al., 2008; WHO, 2012a; Zeliger, 2013; Zheng et al., 2017). Similarly to PCBs, exposure to PBDEs in utero and during early development may cause behavioural disorders in children manifested by sexual dimorphism and learning disabilities (Costa & Giordano, 2007; WHO, 2012a; WHO, 2012b).

Perfluoroalkylated substances (PFASs) are characterized by high chemical and thermal stability and high surface activity and thanks to these properties they are widely used as oleophobic and hydrophobic agents (EFSA, 2008; EFSA, 2012). The most frequently used and, therefore, present in various environmental samples in the largest concentrations are perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) (Góralczyk et al., 2015; WHO, 2012a). Perfluorooctane (PFOA) is a fluorosurfactant that is often used as an emulsifier for the production of fluoropolymers (e.g. Teflon) and as a surfactant in various industries. Perfluorooctane sulfonate (PFOS) is a widely used synthetic surfactant that binds to liver and blood proteins in the human organism. Studies have shown that both compounds may be responsible for lowering the reproductive health of women measured by time to pregnancy (TTP), menstrual cycle disorders, as well as for low birth weight of children (EFSA, 2012; EFSA, 2015; WHO, 2012a; WHO, 2012b). The effect of exposure to PFAS, as in case of PCBs and PBDEs, is often the emergence of metabolic diseases, which are manifested by the occurrence of obesity at an early age, which can lead to the development of type 2 diabetes. In this case, scientists have no clear opinion on the order of emergence of these diseases, i.e. whether obesity causes the appearance of a coexisting disease - diabetes or vice versa (EFSA, 2012; Góralczyk et al., 2015b; Hoyer et al., 2014; WHO, 2012a).

CONCLUSIONS

Using a holistic approach to attempt to describe the relations between the exposure to a variety of different risk factors and response of an organism at the same time, is one of the most serious challenges for the public health. According to the above information, the following conclusions can be made:

Organochlorine pesticides (OCs) are constantly present in the human fat tissue despite the ban on its use since the 80s. Also, PCBs, which were included into so-called ‘Dirty Dozen’ group by Stockholm Convention and have been banned since the beginning of the 90s are still present in the human fat tissue. The presence of those compounds in the organism is related to the internal exposure which is carefully monitored by scientists in the aspect of cumulative risk for toxic effects.

OCs, PCBs and PFASs substances are also detected in human peripheral blood serum, which means that the constant exposure to those compounds is still significant. The exposure may be both external, due to the contact with the polluted environment, including food, and internal, due to the tissue deposits’ release.

Breast milk, which is the best and healthiest baby food that provides a number of benefits, including the psychological ones, also contains androgenic pollutants released from the female organism. In the majority of cases, those pollutants may belong to endocrine active substances (Eds), particularly dangerous during the development of the infant’s hormonal system. Therefore, it is justified to check mother milk for the concentration of POPs, including chloro-, bromo- and fluorinated compounds if during the baby’s development alarming symptoms are observed. The decision to continue breastfeeding ought to be taken on the basis of the tests.

The postnatal exposure in case of persistent organic pollutants from breast milk intake is in some cases dangerously high, which is showed by a very small safety margin for p,p’-DDT intake from breast milk which was assessed on the basis of Estimated Daily Intake (EDI).

The levels of OCs, PCBs and PBDEs in the cord blood have proved that the exposure to those compounds is present also in the prenatal period.

In peripheral blood of women and men the markers of exposure to anthropogenic POPs from the group of organohalogen compounds such as OCs, PCBs and PFASs were discovered.

The results of the biomonitoring have shown the constant presence of those compounds in the human organism, which calls for a necessity to provide proper tools to predict the health risk to people as far as non-professional exposure to environmental pollutants is concerned. Hazard Quotient (HQ) may be used as such a tool.

The conclusions presented above are based on previous studies on possible health consequences due to the constant presence of persistent organic pollutants in human biological material. Numerous toxicological works on the risk of accumulated toxicity and possible interactions between those compounds on the organism level provide worrying data and should prompt all intensive activities aimed at reducing the levels of these compounds in the environment.

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