

**Marek Zieliński**

**Environmental exposure to persistent organic pollutants  
and markers of oxidative stress in women during pregnancy and lactation  
and anthropometric indicators of the newborn**

Dissertation for the degree of Doctor of Medical Sciences

The work was done

at The Department of Biological and Environmental Monitoring  
of Nofer Institute of Occupational Medicine  
under the supervision of Prof. Jolanta Gromadzińska

**ABSTRACT**

PCDD, PCDF and dl-PCB are groups of environmental pollutants which are included among Persistent Organic Pollutants (POPs). Their trace amounts can be found in almost all the spectrum of global ecosystems. Nearly 90% of human exposure to dioxins comes from food. POPs compounds which gather in fatty tissues are slowly metabolized and remain harmful even after relatively long time from the exposure.

Dioxins and dl-PCB gets into the human body with food and accumulate in fat-rich tissues. That is why mother's milk should be considered as the significant channel through which newborns absorb dioxins and dl-PCBs and are exposed to POPs. This exposure comes about in the time when newborns go through the period of rapid growth and development and so they may suffer serious developmental consequences, for instance, inhibition of proper development of the nervous system.

The secretion of dioxins and dl-PCB from mother's milk makes the newborn intake substantial amounts of these compounds to which the mother was exposed throughout her life. Dioxins are compounds which gradually and slowly accumulate in the body. They trigger a number of immunological reactions, which take the form of chronic skin allergies. They can disturb the body hormone economy through induction of the aromatic hydrocarbon receptor. The mechanism of pathogenic interaction between PCDD, PCDF, dl-PCB and tissues and cells is not fully known yet, but we can state for sure that it involves oxidative stress, qualitative and quantitative modifications of cellular receptors or target proteins as well as immunomodulation. There are a number of papers indicating that exposure to 2,3,7,8 tetrachlorodibenzo-*p*-dioxins and other compounds from the POPs group can create oxidative stress observed as the increase in the concentrations of lipid peroxidation products, damaged nucleosides, cracks in the DNA strand and modulated activity of antioxidant enzymes. Dioxins affect child's hormonal systems and hence children in their later life have problems

with obesity, fertility and reproductive disorders, type 2 diabetes, cardiovascular diseases and others.

The purpose of this paper was the search for dependency between the concentrations of polychlorinated dioxins, furans and PCBs in breast milk and the markers of oxidative stress, anthropometric indicators of the newborn and other parameters measured in umbilical and venous blood of mothers. This purpose was achieved by analyzing the aforementioned concentrations of twenty-nine substances taken from milk samples of breast feeding women in the 3 - 8 week of lactation. The estimation of oxidative stress markers in mothers' umbilical and venous blood was also carried out. Two types of dependencies were embarked on. The first one pertained to the relation between the concentrations of polychlorinated dioxins, furans and PCBs in breast milk and the markers of oxidative stress in umbilical and venous blood of mothers. The other focused on the relation between the exposure of the mother during their pregnancy and lactation to polychlorinated dioxins, furans and PCBs and anthropometric indicators of the newborn.

Women with the right course of pregnancy and who have lived in Lodz for at least five years had venous blood samples (n=67) taken just before delivery. The same was carried out with umbilical blood. The following oxidative stress markers were determined: TBARS, oxidative enzymes SOD, GSH-Px1, GSH-Px3, vitamins A and E, trace elements: Se, Zn, Cu, and DNA damage. These women between 3 and 8 week of lactation had milk samples taken. The following were determined in these samples: 7 polychlorinated dibenzo-*p*-dioxins, 10 polychlorinated dibenzofurans and 12 dioxin-like polychlorinated biphenyls. High Resolution Gas Chromatography and High Resolution Gas Spectrometry (HRGC/HRGS) techniques were applied.

Total toxicity equivalent WHO-TEQ<sub>2005</sub> in the tested milk sample was between 0.17 do 15.10 pg/g (per 1g of fat) and the average value was 6.87±3.99 pg/g. The same equivalent for dioxins and furans was between 0.15–11.92 pg/g and for dl-PCB 0.01 – 5.56 pg/g while the relevant averages were 4.98±3.19 pg/g and 1.89±1.49 pg/g respectively. The average concentration of 10 PCDF was 18.54±15.99 pg/g; 7 PCDD 47.20±29.52 pg/g; 12 dl-PCB 5949.03±5194.68 pg/g while maximal determined values were 95.52; 128.26 and 28768.24 pg/g respectively. Compared with the research carried out in other European countries and features in the Fourth Round of WHO Report concerning milk contamination with POP compounds the aforementioned results turned out to be the lowest.

Statistical analysis showed significant dependencies between the concentrations of dioxins and polychlorinated biphenyls and some oxidative stress markers as well as elements and vitamins determined in umbilical and venous blood. Significant statistical correlations were established between the following entities: 1. Concentration of zinc and copper determined in mothers' blood and dioxin sum (p=0.0347) as well as total toxicity expressed by WHO-TEQ (p=0.0124), 2. Concentration of zinc in umbilical blood and the sum WHO-TEQ (p=0.0004), 3. Vitamin A concentration in venous blood and WHO-TEQ PCB (p=0.0263), 4. β-carotene in umbilical blood and 2,3,7,8-TCDD (p=0.0188), 5. Exposure to 2,3,7,8-TCDD and TBARS concentration in venous blood, 6. WHO-TEQ (dioxins) in umbilical blood and SOD activity (p=0.0177), 7. PCDF sum in umbilical blood and umbilical blood GSH-Px erythrocyte activity (p=0.0291), 8. PCCD sum and TBARS concentration in umbilical blood plasma (p=0.0432). Obtained results also indicate the possibility for finding correlations between

them and DNA damage. The results presented in this paper may provide the basis for further studies on the exposure to POP group compounds, especially dioxins, furans and dioxin-like biphenyls, and on the mechanism of their operation.

Morek Zielinski