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Three cycles of human biomonitoring in Flanders − Time trends observed in the Flemish Environment and Health Study

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ABSTRACT

To follow time trends in exposure to environmental chemicals, three successive campaigns of the Flemish Environment and Health Study (FLEHS) have recruited and sampled in total 5825 participants between 2002 and 2014. Cord samples from newborns, urine and blood samples from 14 to 15 years old adolescents and from adults between 50 and 65 years old were analysed in geographical representative samples of the Flemish population. The data of the different campaigns were considered per age group and per biomarker after adjustment for predefined covariates to take into account differences in characteristics of the study populations over time. Geometric means were calculated. Multiple linear regression was used to evaluate time trends. The concentration of serum biomarkers for persistent organic pollutants (POPs), such as marker polychlorinated biphenyls (PCBs), dichlorodiphenyldichloroethylene (p,p'-DDE), the major metabolite of dichlorodiphenyltrichloroethane (DDT), and hexachlorobenzene (HCB) expressed per g lipid, decreased significantly with time. The levels of DDE in all age groups and those of PCBs in cord and adolescent serum samples were almost halved in a time period of ten years. HCB levels were reduced by a factor of 4 in adolescents and in adults. Mean serum concentrations of the more recently regulated perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA) were significantly lower in cord samples of 2013 compared to samples of 2007. The decline was more pronounced for PFOS than for PFOA. In the same period, mean metabolite levels of di-2-ethylhexyl phthalate (DEHP) and of di-*n*-butyl phthalate (DBP) decreased significantly in urine samples of adolescents with sharper declines for DEHP than for DBP. Cadmium and lead levels in cord and adolescent blood samples were significantly lower in the recent campaigns than 10 years before. Also the mean urinary cadmium level in adults was 35% lower

Abbreviations: BMI, body mass index; CL, Confidence Limits; DBP, di-*n*-butyl phthalate; DDT, dichlorodiphenyltrichloroethane; DEHP, di-2-ethylhexyl phthalate; DF, detection frequency; EC, European Commission; EU, European Union; FLEHS, Flemish Environment and Health Study; GM, geometric mean; HCB, hexachlorobenzene; HPLC, High Performance Liquid Chromatography; LOD, limit of detection; LOQ, limit of quantification; MEHHP, mono-2-ethyl-5-hydroxyhexyl phthalate; MEHP, mono-2-ethylhexyl phthalate; MEOHP, mono-2-ethyl-5-oxohexyl phthalate; MnBP, mono-*n*-butyl phthalate; MS, mass spectrometry; PAHs, polycyclic aromatic hydrocarbons; PCBs, polychlorinated biphenyls; PFOA, perfluorooctanoic acid; PFOS, perfluorooctane sulfonate; PIH, Provincial Institute of Hygiene; PM, Particulate Matter; P,p'-DDE, dichlorodiphenyldichloroethylene; POPs, persistent organic pollutants; PSU, primary sampling units; SD, standard deviation; SPE-SAX, Strong Anion Exchange Supra-Clean Spherical Silica-based Solid Phase Extraction; TL, total lipids; t,t'-MA, t,t'-muconic acid; UNEP, United Nations Environment Programme; UPLC, Ultra Performance Liquid Chromatography; VITO, Flemish Institute for Technological research; WHO, World Health Organisation.

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compared to adult samples of 2002. Such favourable trends were not observed for arsenic and thallium measured in cord blood. Similar, the concentrations of 1-hydroxypyrene, a marker for exposure to polycyclic aromatic hydrocarbons (PAHs), was not lower in urine from adolescents sampled in 2013 compared to 2003. In contrast, concentrations of t,t'-muconic acid, a marker of benzene exposure, showed clearly reduced levels. The FLEHS program shows that concentrations of well-regulated chemicals especially traditional POPs and cadmium and lead are decreasing in the population of Flanders. Response to regulatory measures seems to happen rapid, since concentrations in humans of specific regulated perfluorinated compounds and phthalates were significantly reduced in five years time. Biomarker concentrations for arsenic, thallium, and polyaromatic hydrocarbons are not decreasing in this time span and further follow up is warranted.

1. Introduction

Chemicals, including manmade compounds, are a dynamic part of our environment. Even though production and use of many toxic chemicals is regulated, metals and persistent organic pollutants (POPs) continue to circulate through air, water, soil, biota, and humans and are found even in remote areas such as Polar Regions (Donaldson et al., 2010). New chemicals are continuously manufactured and enter the environment through food, consumer products and the use of new technologies. They may end up in waste cycles and can be further recycled (UNEP, 2012; Beck, 2016). Humans are continuously exposed to these chemicals through inhalation, ingestion, and skin contact. It is difficult to adequately control human exposures from various exposure routes. Therefore human biomonitoring programs have been installed in different countries to trace the temporal and spatial distribution of environmental chemicals within the population with priority given to monitoring of the most hazardous chemicals (Choi and Aarø, 2015). Human biomonitoring measures concentrations of chemicals or their metabolites in accessible body fluids or tissues and as such reflects integrated uptake from all exposure routes (Angerer et al., 2007).

In Flanders, the Northern part of Belgium, a human biomonitoring program was installed since 2002. Flanders has 6.6 million inhabitants and is one of the most industrialised areas of Western Europe. Not only does it have a high population density with 479 inhabitants per km^2 in 2016 which is 4 times the average of the European Union, it also has high built surface area with 12.0% of built surface area compared to 1.8% for Europe (European Environment Agency, 2013) and the ecological footprint of the average Flemish citizen fluctuates around 9 global hectares (Flemish Environment Agency, 2015a) for the period 2004–2009, which ranked among the top five globally.

Up to now, three Flemish Environment and Health Study (FLEHS) studies were performed (FLEHS I: 2002–2006, FLEHS II: 2007–2011, FLEHS III: 2012–2015) which included in total 5825 participants. The aim was to measure exposure to hazardous chemicals in a geographically representative sample of the Flemish population. Additional participants were recruited in three hot spot areas in FLEHS II and FLEHS III. To maximise information in relation to the available budget, chemicals were measured in selected age groups taking into consideration their exposure risks and vulnerability. With the third cycle of the program being finished in 2015, it is now possible to evaluate exposure trends over the last 10–12 years.

Chemicals of interest were selected in a transparent and participatory way, based on health and exposure related criteria, such as the seriousness of the expected hazard, potential for bioaccumulation, placental transfer, whether risk information is based on human, animal or mechanistic data, the availability of health based guidance values, the expected margin of safety and whether specific sources for exposure of the general population are known, as well as criteria related to policy relevance, such as whether regulation is already in place and/or whether measures can be taken to reduce exposure. Also technical criteria were considered, such as invasiveness of sampling, the availability of validated analytical methods, the sample volume that is needed, the target population and the analytical costs. Experts from the Flemish Centre of expertise on Environment and Health consisting of research teams from all Flemish universities and two research Institutes (VITO and PIH) and experts from the Flemish Environmental and Health administration and agencies contributed to the scoring. The priority list was further discussed and approved by representatives of the Flemish ministries for environment and health, the Environment and Nature Council of Flanders and the Care, Health and Family Councils.

The first study was considered as a test case that shaped the program. Results of FLEHS I and FLEHS II studies have been extensively reported in Dutch and in English (Flemish Center of Expertise on Environment and Health, 2016; Schoeters et al., 2012a, 2012b).

We measured serum biomarkers for PCBs that were previously mainly used in dielectric, coolant and heat transfer fluids, for the fungicide HCB and for the insecticide DDT. The metabolite p,p'-DDE was measured as a marker for exposure to DDT. The biomarker concentrations in serum lipids reflect the levels that have accumulated in adipose tissues over life time. These hazardous bioaccumulating POPs have been banned since the seventies and are characterised as endocrine disrupting substances, being associated with a wide spectrum of adverse health effects (UNEP/WHO, 2012). Biomarkers for PFOS and PFOA have been measured in serum samples of the two last campaigns. These amphoteric compounds are present in many consumer products that resist stains and oil or repel water. They are persistent and bioaccumulate and are also classified as POPs under the Stockholm Convention (UNEP, 2009). Their use has been restricted more recently. They have been associated with immune and endocrine health effects (Corsini et al., 2014; UNEP/WHO, 2012). Cadmium and lead are measured because of their well-known health effects even at very low concentrations. Cadmium and lead concentrations in blood reflect exposure over the last weeks, urinary cadmium levels are assumed to reflect lifetime exposure. Lead is a known neurotoxicant (Grandjean and Herz, 2015) and cadmium has a wide range of effects including nephrotoxicity, developmental and reproductive effects (Schoeters et al., 2006; Järup and Akesson, 2009). They are classified as carcinogens by the International Agency for Research on Cancer (IARC, 2016). We also included arsenic and thallium in our analysis of blood samples of the two last campaigns. Arsenic is a well-known carcinogen with growing evidence for health effects at very low doses (Carlin et al., 2015). Thallium is widely dispersed in the aquatic environment, it has a toxic potency that is similar to cadmium but it is less well studied (Peter and Viraraghavan, 2005). We included it since no exposure data were available for the Flemish population.