



Maria Assens, Hanne Frederiksen, Anna-Maria Andersson, Anders Juul, Katharina M. Main Department of Growth and Reproduction, Copenhagen University Hospital, Rigshospitalet, Denmark maria.assens.01@regionh.dk

0,10

Introduction and Objective: Very little is known about whether changing habits during pregnancy cause changes in exposure to environmental chemicals. Similarly, little is known of the effect of pregnancy induced metabolic changes on levels of environmental chemicals in biological samples. The objective of this longitudinal study was to describe the variation in exposure of pregnant women to environmental chemicals.

Results: Three UV-filters, the benzophenones (BP-3, 4-HBP, 4-MBP), bisphenol A (BPA), 2-phenylphenol (2-PP), 2 parabens (MeP, n-PrP), metabolites of dibutyl phthalates (MHBP, MiBP, MnBP), di-(2)-

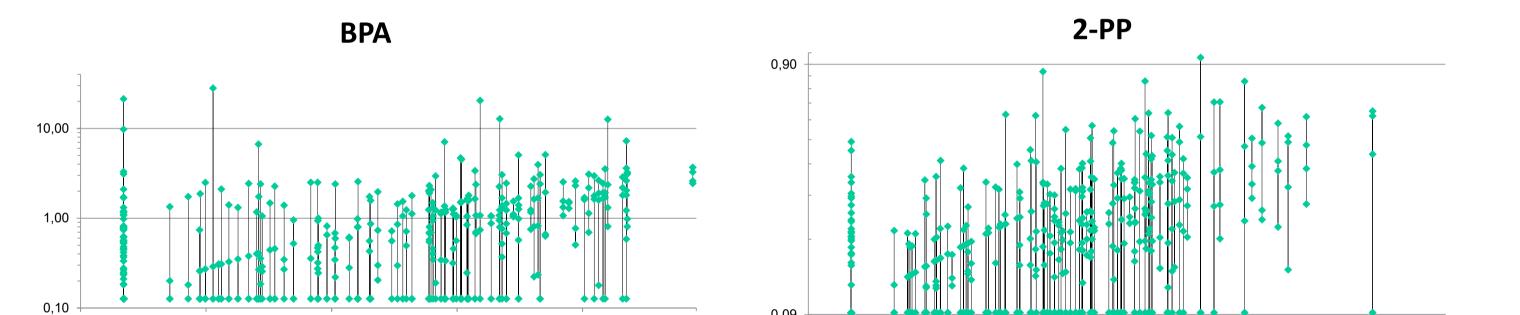
Methods: Serum samples (n=534) collected in 128 pregnant women during 2000-2002 were analyzed for 9 UV filters, 32 metabolites from 15 phthalate diesters, 8 phenols and 7 parabens by TurboFlow-LC-MS/MS. Of the 128 women, 119 had at least 4 samples each corresponding to approximately week 12 (time point 1), 20 (time point 2), 30 (time point 3) and 40 (time point 4).

For chemicals above the limit of detection (LOD) in more than 50% of the samples the Wilcoxon signed-rank test for related samples was used to test differences in concentration at different time points (1-4) during pregnancy. For the same chemicals tests for Intraclass Correlation Coefficients (ICC) were used to examine within-person variance of repeated measures.

Table 1. Concentration (ng/ml) of UV filters (n=532), phthalates (n=534), phenols (n=534) and parabens (n=532) in serum at selected percentiles and at max values.

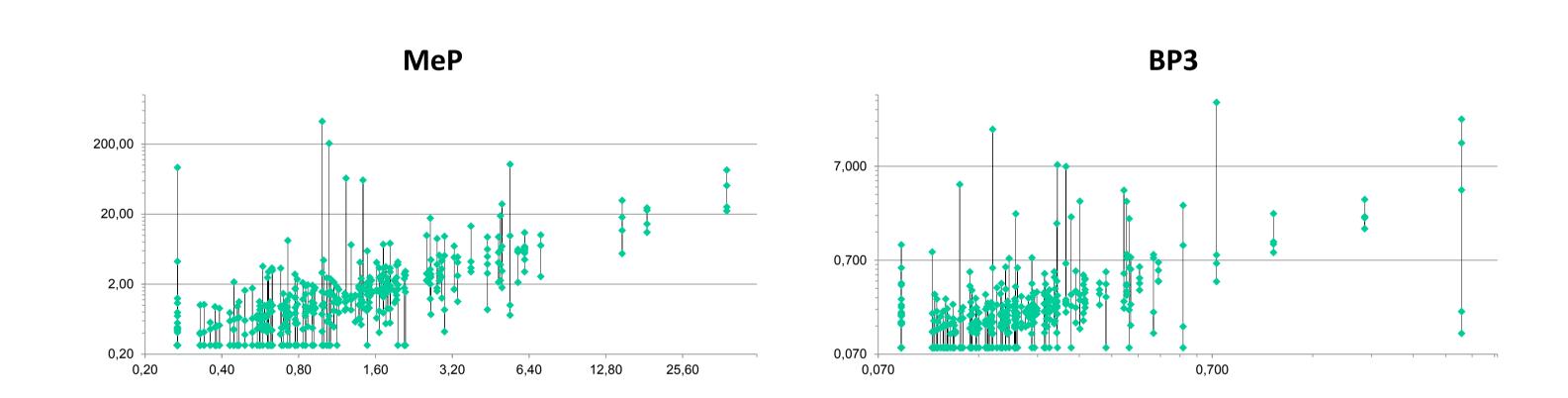
ethylhexyl phthalate (MEHP, MECPP, MCMHP, MEMP) and di-isononyl phthalate (MCIOP, MiNP) and monoethyl phthalate (MEP) and mono-iso-decyl phthalate (MiDP) were detectable in > 50 % of the samples, Table 1. Some individual variation of repetitive measurements are shown in Figure 1. For the three UV filters, 4-HBP, 4-MBP and BP-3 there were significant increases in serum levels during pregnancy between all time points, except from timepoint 3 to 4 for 4-MBP and for timepoint 1 to 2 for BP-3 (4-HBP p<0.001 – 0.002, 4-MBP p<0.001 – 0.001, BP-3 p<0.001 – 0.04). High ICCs for some compounds (n-PrP, 4-HBP, 4-MBP) demonstrated minor within person variance than other compounds with low ICC (Table 2).

Figure 1. Concentrations in individual samples for each woman plotted against the median level of the same woman. Samples with concentration <LOD are set to LOD/V2.



		LOD	10 p	50p	90p	max
Phenols	BPA	0.18	<lod< th=""><th>0.30</th><th>2.2</th><th>28.1</th></lod<>	0.30	2.2	28.1
	2-PP	0.13	<lod< th=""><th>0.14</th><th>0.35</th><th>0.96</th></lod<>	0.14	0.35	0.96
Parabens	MeP	0.38	<lod< th=""><th>0.87</th><th>4.8</th><th>421</th></lod<>	0.87	4.8	421
	n-PrP	0.08	<lod< th=""><th>0.11</th><th>0.68</th><th>19.5</th></lod<>	0.11	0.68	19.5
UV filters	BP -3	0.12	<lod< th=""><th>0.53</th><th>1.18</th><th>22.72</th></lod<>	0.53	1.18	22.72
	4-HBP	0.18	<lod< th=""><th>1.17</th><th>2.10</th><th>3.19</th></lod<>	1.17	2.10	3.19
	4-MBP	0.27	<lod< th=""><th>1.66</th><th>3.62</th><th>5.40</th></lod<>	1.66	3.62	5.40
Phthalates	MHBP	0.47	<lod< th=""><th>0.74</th><th>1.53</th><th>3.04</th></lod<>	0.74	1.53	3.04
	MECPP	0.02	0.14	0.33	0.75	15.29
	MCMHP	0.39	0.79	1.56	3.24	20.08
	MCiOP	0.04	<lod< th=""><th>0.04</th><th>0.29</th><th>3.27</th></lod<>	0.04	0.29	3.27
	MEP *	0.26	0.39	3.23	25.21	173.17
	MiBP*	0.34	0.40	1.30	3.74	20.22
	MnBP*	0.34	0.35	0.93	2.15	22.40
	MEHP*	0.23	1.64	3.03	5.86	38.63
	MiNP*	0.35	0.56	1.31	2.49	5.61
	MiDP*	0.44	<lod< th=""><th>0.80</th><th>4.03</th><th>30.25</th></lod<>	0.80	4.03	30.25

Concentrations of chemicals detectable in more than 50% of samples.



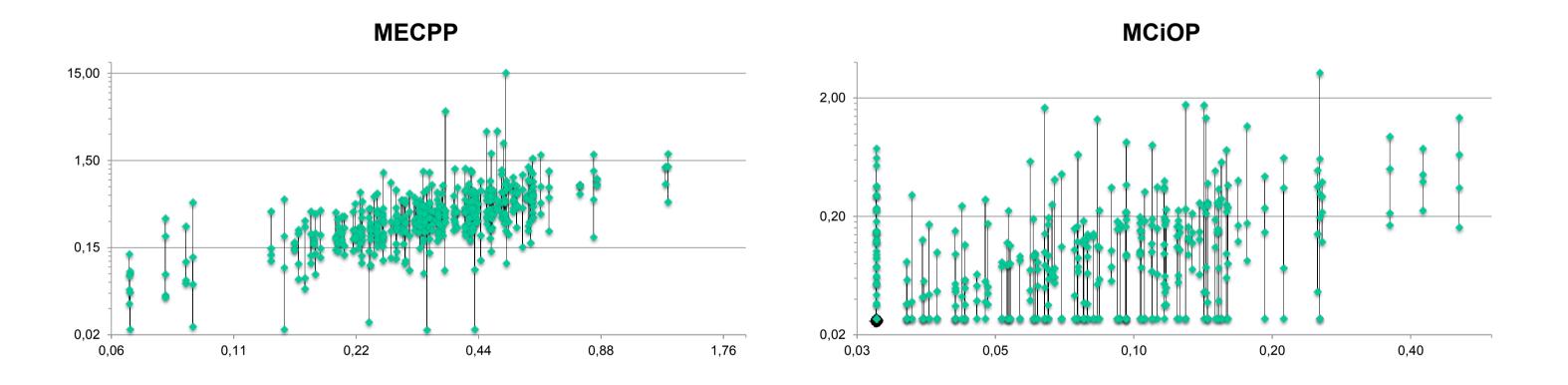


Table 2. Single measures Intraclass Correlation Coefficients (ICC) for chemicals detactable in more than 50% of samples.

*Primary phthalate monoesters are semi-quantitative measurements, because enzymes in serum after sampling theoretically could have hydrolyzed diesters to monoesters and thereby contaminated the samples. LOD = Level of detection

	MeP	n-PrP	BPA	2-PP	BP-3	4-HBP	4-MBP	MHBP	MECPP	МСМНР	MCiOP
ICC	0.027	0.586	0.007	0.149	0.126	0.620	0.786	0.351	0.025	0.133	0.092

Conclusions: Relatively low serum levels and a substantial intra individual variation of the investigated chemicals suggest that serum may not be an optimal matrix to monitor exposure to some of these non persistent chemicals. However, for n-PrP, MeP and MHBP women tended to stay within their individual esposure level throughout pregnancy, whereas concentration for 4-HBP, 4-MBP and BP-3 increased from first to last trimester. Whether this is due to changes in exposures (e.g. change in personal habit) or physiololgical changes (e.g. metabolism/water homeostasis) remains to be explored.

Bibliography:

Frederiksen et al. Correlations between phthalate metabolites in urine, serum, and seminal plasma from young Danish men determined by isotope dilution liquid chromatography tandem mass spectrometry. J Anal Toxicol. 2010 Sep;34(7):400-10. Hart et al. The influence of antenatal exposure to phthalates on subsequent female reproductive development in adolescence: a pilot study. Reproduction. 2014 Mar 2;147(4):379-90. Hines et al. Concentrations of phthalate metabolites in milk, urine, saliva, and Serum of lactating North Carolina women. Environ Health Perspect. 2009 Jan;117(1):86-92.

Centre on endocrine disrupters

