Describing exposures to environmental contaminants in mothers of newborns in France, 2011: first results obtained in the framework of the French biomonitoring program

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Context and aims

As part of the French biomonitoring program, exposure biomarkers were measured in biological samples collected in 2011 from mothers of newborns selected among the participants in the clinical and biological component of the Elfe cohort (Vandentorren et al 2009). The aim was to describe impregnation levels by various chemicals in mothers having given birth in continental France in 2011.

Study population

The study population consists of mothers (>18 years) who gave birth to a single or two living baby, after 33 weeks or more of gestation, in one of the 211 maternity hospitals participating in the biological data collection, between the 27th of June and the 4th of July, or between the 27th of September and the 4th of October, or between the 28th of November and the 5th of December 2011 in continental France, and who were willing to participate in the biological samples collection.

Biological samples and biomarkers measurements

- Cord blood lead
  - Cord blood was sampled in 10 mL EDTA tubes, and stored at +4°C in the hospital. Tubes were then sent (frigo truck) to laboratories in charge of preparing 0.5 mL tubes, that were then frozen. Duration between sampling and freezing did not exceed 36 h. 0.5 mL tubes were then transferred to biobanks where they were stored at -196°C. Samples selected for lead analysis were transported (between -60°C and -80°C, max. duration 24h) to the laboratory in charge of the analysis, and were then stored, protected from light, at -20°C maximum.
  - For each subject, cord blood lead levels were measured in 0.5 mL using inductively coupled plasma mass spectrometry (ICP-MS). Quality controls, blanks and measurements in reference materials were performed to assess metrological quality of the measurements. Limit of detection (LOD) was 0.6 µg/L, and limit of quantification (LOQ) was 2 µg/L.
- Hair mercury
  - A strand of hair was cut in the occipital area of the mother's head. It was then stapled to a card, noting the orientation (tip / root) of the strand. Cards were individually placed in envelopes, and were stored and transported at ambient temperature. Samples selected for mercury analysis were sent (by airpost) to the laboratory in charge of the analysis.
  - For each subject, hair mercury levels in the 3 cm of the strand closest to the root (representing at least 5µg of hair) were measured using cold vapor atomic absorption spectroscopy (AAS). Quality controls, blanks and measurements in reference materials were performed to assess metrological quality of the measurements. LOD was 0.04 µg/g, and LOQ was 0.14 µg/g.
- Urinary BPA
  - Pregnant women provided spot urine sample just after their admission to maternity. Urine was collected in 200 mL polypropylene containers and stored at +4°C. Samples were then aliquoted in four 10 mL tubes and ten 2 mL tubes and frozen at -20°C. Duration between sampling and freezing did not exceed 36 h. Tubes were then transferred to biobanks where they were stored at -80°C, until the transportation of selected samples to the laboratory that carried out the urinary BPA determination (<-60°C, 24 h). In the laboratory, samples were stored at -20°C and protected from light.
  - Urinary free BPA and total BPA (free and conjugated) were quantified by Gas Chromatography coupled to tandem Mass Spectrometry (GC/MS/MS). The analytical method required one 10 mL urine sample for each subject. Quality controls, blanks and measurements in reference materials were performed to assess metrological quality of the measurements. A subset of water samples (n=10) having been processed the same way as urinary samples was analyzed to rule out external contamination. LOD was 0.1 µg/L and LOQ was 0.3 µg/L. Urinary creatinine was determined by the Jaffé method.

Statistical analysis

For each biomarker, the geometric mean, median, and percentiles of the biomarkers levels distribution were estimated, taking into account the sampling design and adjusting via calibration, in order to obtain estimates representative of mothers having given birth in continental France in 2011.

Left-censored data (chemical levels below the LOD or LOQ) were replaced by imputed values, using multiple imputation by chained equations method. Because the imputed values cannot be treated as actual measured data, the imputation process was repeated several times to create multiple complete data sets. Each complete data set was analysed, and the results were combined to account for the uncertainty resulting from Multiple Imputation methods.

The statistical analysis was conducted using STATA version 12 and the SURVEY package in R version 3.1.0.

Results

- **Lead**

Overall, 1,968 women were included for the analysis of cord blood lead levels. All samples were above LOD, and 99.5% were above LOQ.

TABLE 1 Distribution (Geometric mean – GM, and percentiles) of cord blood lead level (µg/L) in mothers having given birth in 2011, Continental France

	n	GM	CI 95% GM	P10	P25	P50	P75	P90	P95	CI 95% P95
Total	1,968	**8.30**	[7.94;8.68]	4.18	5.57	7.78	11.4	17.5	**24.3**	[20.7;27.1]
Age (years)										
≤24	291	6.99	[6.57;7.45]	3.96	5.13	6.85	9.45	12.4	15.2	[12.6;21.0]
25-29	679	8.01	[7.62;8.41]	4.08	5.48	7.42	11.3	16.6	23.4	[19.2;28.3]
30-34	660	8.39	[7.97;8.84]	4.30	5.94	7.92	11.0	16.4	23.4	[18.4;27.0]
≥35	311	9.55	[8.45;10.8]	4.28	6.02	9.17	14.7	21.6	29.4	[21.6;40.5]

- **Mercury**

Overall 1,799 women were included for the analysis of hair mercury levels. 97.6% of the samples were above LOD, and 90.9% were above LOQ.

TABLE 2 Distribution (Geometric mean – GM, and percentiles) of hair mercury level (µg/g) in mothers having given birth in 2011, Continental France

	n	GM	CI 95% GM	P10	P25	P50	P75	P90	P95	CI 95% P95
Total	1,799	**0.395**	[0.370;0.422]	0.127	0.242	0.424	0.722	1.10	**1.39**	[1.30;1.51]
Age (years)										
≤24	232	0.263	[0.230;0.303]	0.088	0.159	0.282	0.444	0.769	0.958	[0.764;1.14]
25-29	562	0.365	[0.332;0.402]	0.117	0.236	0.367	0.657	1.02	1.36	[1.17;1.52]
30-34	641	0.440	[0.395;0.487]	0.133	0.280	0.503	0.821	1.18	1.50	[1.30;1.76]
≥35	358	0.494	[0.454;0.536]	0.194	0.318	0.547	0.772	1.24	1.47	[1.37;1.61]

- **BPA**

Overall, 1,764 women were included for the analysis of urinary BPA levels. For free BPA, only 33% of the samples were above LOD, and 10.7% were above LOQ. For total BPA, 90.2% were above LOD, and 73.8% were above LOQ. Because of the high percentage of left censored values for free BPA, results below only concern total BPA.

TABLE 3 Distribution (Geometric mean – GM, and percentiles) of total BPA urinary levels and creatinine-adjusted levels in mothers having given birth in 2011, Continental France

	n	GM	CI 95% GM	P10	P25	P50	P75	P90	P95	CI 95% P95
Unadjusted BPA (µg/L)										
Total	1,764	**0.690**	[0.643;0.740]	<LOQ	0.303	0.747	1.63	3.10	**5.28**	[4.50;6.72]
Age (years)										
≤24	251	0.801	[0.692;0.923]	<LOQ	0.410	0.888	1.89	3.43	4.78	[3.73;7.97]
25-29	589	0.730	[0.645;0.830]	<LOQ	0.321	0.791	1.67	3.48	5.20	[4.31;6.84]
30-34	620	0.594	[0.519;0.681]	<LOQ	<LOQ	0.691	1.53	2.78	5.43	[3.48;7.26]
≥35	285	0.726	[0.620;0.847]	<LOQ	0.317	0.690	1.62	3.02	5.87	[3.84;9.50]
Creatinine-adjusted BPA (µg/g)										
Total	1,764	**0.869**	[0.818;0.925]	<LOQ	0.430	0.919	1.74	3.32	**6.03**	[4.77;7.03]
Age (years)										
≤24	251	0.928	[0.818;1.050]	<LOQ	0.490	0.996	1.89	3.12	5.25	[3.18;7.67]
25-29	589	0.891	[0.799;0.997]	<LOQ	0.425	0.936	1.75	3.40	5.87	[4.33;7.46]
30-34	620	0.763	[0.685;0.850]	<LOD	<LOQ	0.824	1.54	3.07	4.99	[3.67;7.10]
≥35	285	0.985	[0.851;1.14]	<LOQ	0.460	1.000	1.88	4.17	6.71	[4.46;8.23]

Discussion

Lead and mercury have well known toxic properties, and thus reference values for impregnations exist for general population and/or pregnant women. In the present study, two subjects had cord blood lead level over the French reference value for blood lead level in pregnant women (100 µg/L), and two subjects had hair mercury levels over the WHO reference value (10 µg/g).

Cord blood lead levels were lower than those observed in previously published studies, both in France and in other countries.

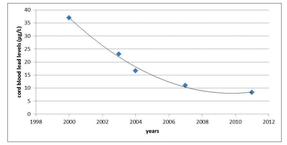
TABLE 4 Blood lead levels observed in previously published studies in France and abroad

Country (ref.)	Year (data collection)	Population	n	Biological sample	LOQ (µg/L)	Geometric mean (GM) or median (med) (µg/L)	% >LOQ
France (Smargiassi *et al.* 2002)	2000	Pregnant women Paris	100	Cord blood	NA	GM = 37	NA
France (Yazbeck *et al.* 2006)	2003-2004	Pregnant women Paris suburbs	1,029	Cord blood	5	GM = 16.6	~90%
France (Gottot *et al.* 2014)	2003	Pregnant women Paris	677	Cord blood	20	med = 23	NA
France (Vandentorren *et al.* 2013)	2007	Pregnant women Paris suburbs and Rhône-Alpes	236	Cord blood	2	GM = 11	100%
Spain (Llop *et al.* 2011)	2003-2007	Pregnant women	1,466	Cord blood	20	GM = 10.6	5.9%
Belgium (Koppen *et al.* 2009)	2002-2006	Pregnant women	1,107	Cord blood	2	GM = 13.1	96%
Belgium (Zhang *et al.* 2012)	2008	Pregnant women	220	Cord blood	10	NA	47.3%
France (Fréry *et al.* 2011)	2006-2007	Women aged 18-45 years	584	Blood	10	GM = 16.66	96

NA: not available

This decrease over time in lead exposure could be related to curbing of atmospheric lead sources (industrial emitters and vehicles, in relation with substitution of lead as an anti-explosive agent in gasoline).

FIGURE 1 Temporal decrease in lead concentrations measured in cord blood in France from 2000 to 2011



Hair mercury levels were similar or lower than those observed in previously published studies, both in France and in other countries.

TABLE 5 Hair mercury levels observed in previously published studies in France and abroad

Country (ref.)	Year (data collection)	Population	n	Biological sample	LOQ (µg/L)	Geometric mean (GM) or median (med) (µg/L)	% >LOQ
France (Drouillet-Pinard *et al.* 2010)	2003-2006	Pregnant women Nancy, Poitiers	665	Hair	NA	med = 0.52	NA
France (Chevrier *et al.* 2013)	2004-2007	Pregnant women Brittany	318	Hair	0.02	P33 = 0.48	NA
France (Albert *et al.* 2010; Pouzaud *et al.* 2010)	2005-2006	Pregnant women 3rd trimester Nantes	137	Hair	NA	GM = 0.79	NA
France (Fréry *et al.* 2011)	2006-2007	Women aged 18-45 years	126	Hair	0.01	GM = 0.53	100%
France (Cordier *et al.* 1998)	1994	Pregnant women French Guyana	109	Hair	NA	GM = 1.6	NA
Belgium (Belgian Steering Committee on HBM 2013)	2011-2012	Women aged 18-45	129	Hair	NA	GM = 0.383	95.3%
Belgium (Croes *et al.* 2014)	2008-2009	Pregnant women	255	Hair	NA	GM = 0.34	NA
Italy (Valent 2013)	2007-2009	Pregnant women 20-22 GW	604	Hair	NA	med = 0.788	NA

NA: not available

Urinary BPA levels were lower than those observed in previously published studies, both in France and in other countries, conducted before 2010 (year of the first restrictions on feeding bottles which contained BPA). These levels were consistent with recent results from Canada.

TABLE 6 BPA levels observed in previously published studies in France and abroad

Country (ref.)	Year (data collection)	Population	n	Biological sample	LOQ (µg/L)	Geometric mean (GM) or median (med) (µg/L)	% >LOQ
France (Vandentorren *et al.* 2013)	2007	Pregnant women Paris suburbs and Rhône-Alpes	254	Urine	0.1	GM = 2.5	91.7%
France (Philippat *et al.* 2014)	2003-2006	Pregnant women Nancy, Poitiers	520	Urine	0.4	med = 2.5	99%
Spain (Casas *et al.* 2013)	2004-2006	Pregnant women 3rd trimester	479	Urine	0.1	GM = 1.8	99.4%
Norway (Ye *et al.* 2009)	1999-2004	Pregnant women	110*	Urine	0.26	GM = 2.81	NA
Netherlands (Ye *et al.* 2008)	2004-2006	Pregnant women Rotterdam	100	Urine	0.26	GM = 1.1	82%
United-States (Harley *et al.* 2013)	1999-2000	Pregnant women California	402	Urine	0.4	GM = 1.1	~82%
Canada (Arbuckle *et al.* 2014)	2008-2011	Pregnant women 1st trimester	1,936	Urine	0.2	GM = 0.80	87.7%

** Analyzes were conducted on ten pooled specimens, each comprising one 1 mL urine sample from 11 women.*

Conclusion

In conclusion, first results obtained in the framework of the French biomonitoring program for lead, mercury and BPA indicate that levels measured in 2011 among parturient women tend to be similar or lower than those observed in other countries. Results for other chemicals, including phthalates, pesticides, other metals, brominated flame retardants and perfluorinated compounds will be available next, as well as multivariate analyses in order to identify main determinants of these chemical levels.

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