Exposures to environmental contaminants in mothers of newborns in France, 2011

HBM in the Elfe Birth Cohort – Results to date

Clémentine DEREUMEAUX, Laurence GULDNER , Abdesattar SAOUDI, Marie PECHEUX, Bénédicte BERAT, Vérène WAGNER, Sarah GORIA, Serge BRUNEL, Perrine DE CROUY-CHANEL, Clémence FILLOL, Amivi OLEKO, Stéphanie VANDENTORREN, Alain LE TERTRE, Nathalie VELLY, Corinne DELAMAIRE, Agnès LEFRANC, Sébastien DENYS

Department of Environmental Health, French Institute for Public Health Surveillance

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Context of the French HBM program

- **Launching:** included in a French law (08/2009)
- **Implementation:** an action of the 2nd French national environment and health plan (2009-2013)
- This program currently consists in 2 cross-sectional human biomonitoring surveys :
  - **A perinatal component** based on a selection of mothers of newborns enrolled in the Elfe* cohort
  - A general population survey coupled with health examinations and with a nutritional component : Environment, Health, Biomonitoring, physical Activity, Nutrition (**Esteban)**

** Elfe is the acronym for "Étude longitudinale française depuis l'enfance" (French Longitudinal Study since Childhood)*

Aims of the perinatal component of the French biomonitoring program

- **Describe internal exposure** to some environmental contaminants among pregnant women giving birth in continental France in 2011
- **Compare** the results with previous surveys conducted in France (ie ENNS for general population) and abroad (e.g. in other European or American HBM programs)
- **Identify the determinants** of exposure when possible

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Study design

- **Method**: cross-sectional study within a cohort (Elfe)
- **Sample size**: **4,145 mothers of newborns** selected among the participants in the clinical and biological component of the Elfe cohort (a national representative cohort of 18,000 children born in 2011)
- **Recruitment**:
  - ✓ **Adult mothers** (> 18 years) **living in continental France**
  - ✓ Giving birth
    - **during one of the 3 intake periods** between **June-December 2011** ,
    - after >= **33 weeks of gestation**,
    - in one of the **211 maternity hospitals** participating in the biological data collection of Elfe
  - ✓ **Able to understand and sign a consent form**
  - ✓ Having at least **one biological sample available**

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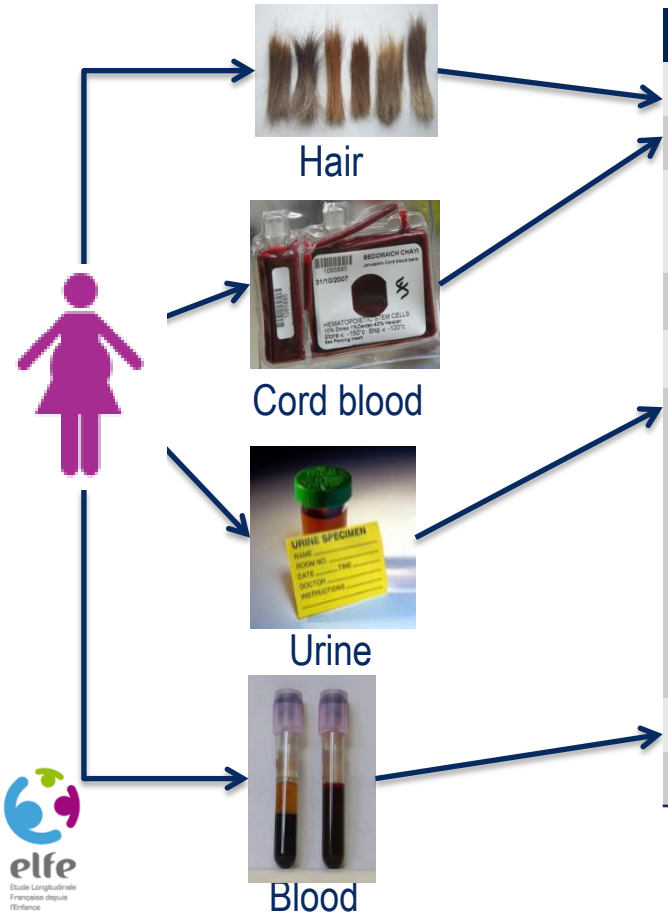
Data collection

- **Questionnaires:** face-to-face interview and self-administered questionnaires at maternity
- **Sample collection and biomarkers measurements:**



Biological sample	Biomarkers	n
Hair	Mercury	1,799
Cord blood	Lead	1,968
Urine	Other metals (Al, As, Cd, Co, Cr, Cs, Ni, Sb, Sn, U, V)	990
Urine	Bisphenol A	1,764
Urine	Phthalates	989
Urine	Pyrethroid	1,077
Urine	Other pesticides (atrazine, glyphosate, propoxur, chlorophenols and organophosphorous insecticides)	1,036
Serum	Dioxin, furan and PCB	208
Serum	Brominated flame retardants	277
Serum	Perfluorinated compounds	277

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Statistical analysis

- **Sampling design:** stratification with two degrees (maternity and mother of newborn)
- **Imputation of missing data** (no response to the questionnaire or left-censored biomarker levels) by Multiple Imputation method (ICE : STATA module)
- After treatment of total nonresponse, **estimations are representative of mothers having given birth in continental France in 2011** (except for dioxin, furan, PCB, BFR and PFC)
- **Results:**
  - ✓ For each biomarker, the **geometric mean**, **median** and **percentiles** of the biomarker levels distribution have been estimated
  - ✓ **Multivariate analyses** were conducted to search for determinants of biomarkers levels using a generalized additive model

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Phtalates (n=922, urine)

Biomarqueur		%>LOQ	MG	IC95%MG	P95	IC 95 % P95
DnBP	MnBP	82,2	5,0	[4,0 ; 6,2]	236,3	[170,4 ; 324,3]
DiBP	MiBP	83,1	4,3	[3,5 ; 5,4]	221,7	[161,5 ; 288,3]
BBzP	MBzP	66,6	0,8	[0,7 ; 1,0]	42,8	[32,2 ; 57,9]
DEP	MEP	90,2	35,4	[27,4 ; 45,4]	2 083,8	[1 341,5 ; 2 948,3]
DEHP	MEHP	70,8	1,6	[1,4 ; 1,8]	37,2	[28,8 ; 53,6]
	MEOHP	61,2	0,8	[0,7 ; 1,0]	45,0	[33,5 ; 57,8]
	MEHHP	69,1	1,2	[0,9 ; 1,4]	57,3	[41,5 ; 81,4]
	MECPP	80,2	3,0	[2,5 ; 3,7]	93,9	[59,1 ; 121,4]
	ΣDEHP*	-	7,4	[6,2 ; 8,6]	177,1	[137,3 ; 312,0]
DiNP	MHiNP	70,4	2,1	[1,7 ; 2,6]	91,0	[70,3 ; 106,2]
	MOiNP	18,0	NC†	-	8,8	[4,7 ; 12,7]
	MCiOP	82,2	5,2	[4,2 ; 6,3]	165,9	[131,2 ; 200,9]
	ΣDiNP**	-	11,0	[9,1 ; 13,0]	276,9	[214,9 ; 320,9]

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Phtalates – Main Data

- At least one compound quantified in 99.6% of the population
- Mean concentration range from 7.4 µg L (DEHP metabolites, PVC products) to 35 µg L (DEP metabolite, hygien product)
- DEHP : 16 women above HBM-I (300 µg/L)
- Lower levels than previous French studies
- Levels are higher for consumers of food in contact with packages containing plastics, hygien products and paint during pregnancy

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BPA (n = 1764, urine)

Biomarker	%>LoD	GM	CI95% GM	P95	CI 95 % P95
Bisphenol A (µg/L)					
Bisphenol A total	90.2	0.69	[0.64 ; 0.74]	5.3	[4.5 ; 6.7]
Bisphenol A free	33.0	NC	-	0.6	[0.5 ; 0.6]

- None > HBM-1 (200 µg BPA_{tot} /L)
- Levels lower than previous studies
- Positive association with :
  - ✓ Consumption of food stored in plastic containers
  - ✓ TV watching and PVC at home : proxy for indoor air and household dust

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Pesticides (n = 1077, urine)

Pesticides (µg/L urine)					
Biomarker	%>LoD	GM	CI95% GM	P95	CI 95 % P95
Atrazine	0.0	NC	NC	< LOQ	NC
A. mercapturate	0.9	NC	NC	< LOQ	NC
A. desethyl	0.0	NC	NC	< LOQ	NC
A. desisopropyl	0.0	NC	NC	< LOQ	NC
A. desethyl desisopropyl	0.0	NC	NC	< LOQ	NC
A. hydroxy	1.0	NC	NC	< LOQ	NC
A. hydroxy desethyl	0.0	NC	NC	< LOQ	NC
A. hydroxy desisopropyl	0.0	NC	NC	< LOQ	NC
A. hydroxydesethyldesisopropyl	0.1	NC	NC	< LOQ	NC
Glyphosate	0.3	NC	NC	< LOQ	NC
Ampa	0.2	NC	NC	< LOQ	NC
Propoxur	4.3	NC	NC	< LOQ	NC
2 IPP	21.0	NC	NC	0.249	[0.2 ; 0.3]
Chlorophenols					
4-MCP	1.8	NC	NC	< LOQ	NC
2,4 DCP	10.7	NC	NC	0.2	[<LOQ ; 0.4]
2,5 DCP	9.6	NC	NC	< LOQ	NC
2,4,5 TCP	0.8	NC	NC	< LOQ	NC
2,4,6 TCP	3.0	NC	NC	< LOQ	NC
Organophosphorous insecticides					
PCP	11.3	NC	NC	< LOQ	NC
DMP	28.5	NC	NC	64.4	[43.7 ; 95.1]
DETP	28.5	NC	NC	2.5	[2.0 ; 3.1]
DMTP	10.2	NC	NC	2.5	[1.3 ; 3.8]
DMDTP	8.5	NC	NC	4.2	[2.3 ; 6.4]
DEP	4.3	NC	NC	< LOQ	NC
DEDTP	0.0	NC	NC	< LOQ	NC

Atrazin
Glyphosate
Propoxur
Chlorophenols
Organophosphorus

Low Q levels

(up to 30% for DMP and DETP)

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Pesticides – case of Pyrethroids

Pyrethroid (µg/L urine)					
Biomarker	%>LoD	GM	CI95% GM	P95	CI 95 % P95
3 PBA	100.0	0.4	[0.3 ; 0.4]	1.9	[1.6 ; 2.2]
F PBA	8.2	NC	NC	0.02	[<LOQ ; 0.3]
Br2CA	99.8	0.2	[0.2 ; 0.3]	1.4	[1.3 ; 1.5]
Cis-DCCA	99.9	0.2	[0.1 ; 0.2]	0.9	[0.8 ; 1.0]
Trans-DCCA	99.8	0.3	[0.2 ; 0.3]	2.3	[1.6 ; 2.7]

Apart from F PBA: almost 100% detection level

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Pesticides – Main Data

- % > LOQ : Gradient among the monitored substances and their metabolites :

  Pyrethroids - 100%

  Organophosphorus - 50%

  Propoxur 4%; 2-IPP - 20%

  At least one chlorophenol metabolite - 10 %

  Herbicids atrazin and metabolites or glyphosate and metabolites < 1%

- Levels lower than previous French studies
- Pyrethroids: Overexposure of this population, as compared to US (idem as the ENNS study for the general population)
- Level increased with domestic use, alcohol, exposure to tobacco, and proximity to agricultural harvests

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PCDD/F, PCB dl and PCB(n = 208, serum)

Dioxin & furan (pg/g lipid)*					
Biomarker	%>LQ	GM	CI95% GM	P95	CI 95 % P95
Dioxin	0-100	99.5	[91.7 ; 108.0]	233.0	NC
Furan	0-100	14.0	[13.4 ; 14.6]	20.5	NC
∑PCDD/PCDF	-	115.0	[105.0 ; 127.0]	237.0	NC
PCB (ng/g lipid)*					
PCB dioxin-like	0-100	9.3	[8.6 ; 9.9]	21.6	NC
PCB total	0-100	82.5	[76.4 ; 88.5]	210.0	NC

- Non-weighted results : just descriptive
- At least one compound detected in 100% of the population
- Lower values than previous F or EU studies

But higher than Amercian values (idem as ENNS vs Nhanes)

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Metals and metalloids

- Aluminium*, Antimony, Arsenic, Cadmium, Caesium, Chromium, Cobalt, Lead, Nickel, Stain, Uranium, Vanadium
- urines
- N= 990 mothers

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Levels of metals and metalloids in urines (µg/L)

Biomarqueurs	%>LD	MG	IC95% MG	P95	IC 95 % P95
Aluminium	NV*	NV	NV	NV	NV
Antimoine	94,3	0,040	[0,036 ; 0,045]	0,194	[0,180 ; 0,205]
Arsenic	100,0	11,04	[10,12 ; 11,89]	59,43	[48,42 ; 70,00]
Cadmium	99,3	0,12	[0,11 ; 0,13]	0,49	[0,41 ; 0,54]
Césium	100,0	4,93	[4,64 ; 5,25]	14,96	[13,51 ; 16,26]
Chrome	96,6	0,30	[0,27 ; 0,34]	1,74	[1,37 ; 2,05]
Cobalt	100,0	0,85	[0,80 ; 0,91]	3,11	[2,83 ; 3,42]
Etain	93,2	0,29	[0,25 ; 0,33]	2,82	[2,19 ; 3,66]
Nickel	99,2	1,38	[1,30 ; 1,47]	4,96	[4,37 ; 5,52]
Uranium	60,9	NC**	NC	0,02	[0,02 ; 0,03]
Vanadium	98,7	0,28	[0,25 ; 0,31]	1,41	[1,02 ; 1,95]

**NV = Non validated*

*** NC = Non calculated due to high censor (>40%)*

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Metals – Ex on Sb, As and Cd

- **Antimony**
  - same order of magnitude than levels observed for the F general population and lower that US or spanish levels for comparable population
- **Total Arsenic**

  American (2009-2011) : 8,3 µg/g creatinine (Nhanes/ECMS)

  General F Women population (ENNS) : 12 µg/g creatinine

  This study : 15, 05 µg/g creatinine

  ✓ Levels increase with fish and sea products consumption
- **Cadmium**

  This study : 0,12 µg/L

  General F Women population (ENNS) : 0,29 µg/L

  Canadian (Women 20-39 y old) : 0,35 µg/L

  ✓ Levels increase with BMI, age, root vegetable consumption

  no fish consumption and smoking (non significant)

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Conclusion and perspectives

- First representative concentrations of many chemicals of public concern for a sensitive population at the French Population level

- Comparisons are limited by methodological limits due to different protocols designs among studies but
  - Allow to estimate the French level of exposure as compared to other countries
  - Provide insight of a downward trend in exposure to several chemicals : Atrazin, PCDD/F, BPA, phtalates, organophosphorus pesticides
  - Overexposure as compared to US population for PCB and Pyrethroïds
- levels : mainly consistent with the litterature

- Perspectives : what does it mean in terms of health impact ?
  - links with children development
  - development of exposure reference values
  - links with toxicology and external exposure

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