



Exposure to food contaminants during pregnancy

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ABSTRACT

During pregnancy, the fetus is exposed to contaminants from its mother's diet. This work provides an assessment of the dietary exposure of pregnant women to inorganic contaminants (aluminum, mercury, lead, inorganic arsenic, cobalt), polychlorodibenzodioxins, polychlorodibenzofurans, dioxin-like and non-dioxin-like polychlorobiphenyls (DL-PCBs, NDL-PCBs), polybromodiphenyl ethers (PBDEs), perfluoroalkyl acids, mycotoxins (zearalenone, patulin, trichothecenes), and heat-generated compounds (acrylamide and polycyclic aromatic hydrocarbons).

Consumption data of 2002 pregnant women aged 18 to 45 from the EDEN cohort study were combined with contamination data from the second French total diet study to assess the exposure before pregnancy ($n = 1861$) and during the third trimester of pregnancy ($n = 1775$). Exposure was also assessed considering the season during which the third trimester of pregnancy occurred.

Significant changes in consumptions during pregnancy and between seasons were associated with differences in exposures for some substances.

Some contaminant exposures appeared to be of health concern. Margins of exposure to acrylamide (635 to 1094 for mean), inorganic arsenic, lead, and BDE-99 (≤ 100) were too low to exclude all risks. For NDL-PCBs, T-2 and HT-2 toxins, and deoxynivalenol, significant exceedings of toxicological reference values were found before pregnancy, but there was no significant exceeding in the third trimester.

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1. Introduction

It is well known that maternal environment has implications for fetus health. The fetus is transplacentally exposed to contaminants in food and in the environment (Katić et al., 2010). It is particularly vulnerable to toxicants, which could disrupt developmental processes (Wigle et al., 2006). Some contaminants have been known to cause specific harms for both the mother and the fetus. Among them, this work will focus on those of concern for contamination from food intake i.e. trace elements (aluminum, inorganic mercury and methylmercury, lead, inorganic arsenic and cobalt), polychlorodibenzodioxins (PCDDs), polychlorodibenzofurans (PCDFs), dioxin-like and non-dioxin-like

polychlorobiphenyls (DL-PCBs and NDL-PCBs), perfluoroalkyl acids (perfluorooctane sulfonate (PFOS), and perfluorooctanoic acid (PFOA)), mycotoxins (zearalenone, patulin, trichothecenes), heat-generated compounds (acrylamide and polycyclic aromatic hydrocarbons (PAHs)) and brominated flame retardants (polybromodiphenyl ethers (PBDEs)).

Most of these chemicals have been associated with adverse effects during pregnancy or in the child development. Lead exposure may cause increased risk of pregnancy hypertension and miscarriage (Yazbeck et al., 2009). PCDD/Fs and PCBs, inorganic arsenic, lead, and methylmercury have been associated with reduced length of gestation or preterm birth (Givens et al., 2007; Miranda et al., 2011; Rahman et al., 2007; Vigeh et al., 2011; Yazbeck et al., 2009). In animal experiments, inorganic mercury reduced implantation efficiency and decreased live birth rate (JECFA, 2011). Acrylamide exposure increases the rate of spontaneous abortion and neonatal mortality (El-Sayyad et al., 2011), as well as inorganic arsenic (Rahman et al., 2007), and decreases the body weight of the fetus (Duarte-Salles et al., 2013; El-Sayyad et al., 2011; Pedersen et al., 2012), so do PCDD/Fs, PCBs, and mycotoxins (Doi et al., 2008; Givens et al., 2007; Hepworth et al., 2012; Khlangwiset et al., 2011). Developmental delay or neurotoxic effects have also been reported for exposure to methylmercury (Dorea and Donangelo, 2006; Miranda et al., 2011),

Abbreviations: EFSA, European Food Safety Authority; FFQ, food frequency questionnaire; PCDD, polychlorodibenzodioxin; PCDF, polychlorodibenzofuran; DL-PCB, dioxin-like polychlorobiphenyls; HBGV, health-based guidance value; INCA, French individual and national food consumption survey; JECFA, Joint FAO/WHO Expert Committee on Food Additives; LB, lower-bound; LOD, limit of detection; LOQ, limit of quantification; MOE, margin of exposure; NDL-PCB, dioxin-like polychlorobiphenyl; PAH, polycyclic aromatic hydrocarbon; PBDE, polybromodiphenyl ethers; PFOA, perfluorooctanoic acid; PFOS, perfluorooctane sulfonate; TDS, total diet study; TRV, toxicological reference value; UB, upper-bound.

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aluminum (Colomina et al., 2005), PCDD/Fs and PBCs (Halldorsson et al., 2009), perfluoroalkyl acids (Olsen et al., 2009), PAHs (Edwards et al., 2010), and PBDEs (Gascon et al., 2011; Wan et al., 2010). Furthermore, perfluoroalkyl acids and some mycotoxins have been shown to be related to perturbation in the structure of the immune system of the child (Doi et al., 2008; Fei et al., 2010; Khlangwiset et al., 2011). Moreover, acrylamide has been shown to have carcinogenic potential (JECFA, 2011). Genotoxicity has also been reported for aluminum and cobalt (ANSES, 2011; IARC, 1997), and the T-2 toxin (Doi et al., 2008).

Risk assessment linked with these contaminants is usually done by calculating dietary exposures, and comparing these exposures to toxicological reference values (TRVs). The TRVs are established by international agencies such as the Joint FAO/WHO Expert Committee on Food Additives (JECFA) or the European Food Safety Authority (EFSA) in order to protect the most sensitive population, such as the fetus. Knowing the exposure of women during pregnancy is crucial in order to predict how it could affect their child's health.

An estimation of this exposure can be made using the total diet studies (TDS) that have been conducted in various countries among the general population (ANSES, 2011; FSANZ, 2011; Health Canada, 2009; US-FDA, 2010). These studies aim at giving an accurate and realistic view of dietary exposure to major contaminants for the purpose of quantitative risk assessment. A TDS consists in purchasing foods commonly consumed by a population (based on information obtained through national dietary surveys), processing them as for consumption, pooling them into food composite samples, and analyzing these samples for contaminants (EFSA, 2011c). TDSs are usually designed to measure the background intake of chemicals by different age/sex groups of a country. More particularly, in France, the exposure of women of childbearing age has been calculated in the second TDS and could be considered close to the exposure during pregnancy.

However, diet changes usually occur during pregnancy: women will eat foods that they are not used to, or in contrary avoid others that they consumed a lot before getting pregnant; the quantities eaten could also vary (Crozier et al., 2009). These changes could be either chosen by women who want to eat "better" for the sake of their child (Gardner et al., 2012), or could be related to the hormonal changes of pregnancy (Faas et al., 2010). Season could also be a cause of change in the consumption habits of pregnant women (Prasad et al., 2010). So, it seems important to study precisely the food intakes of pregnant women to better assess contaminant dietary exposure.

This study will focus on (i) describing the diet before and during pregnancy, (ii) assessing the exposure to the contaminants listed above due to food intakes, before and during pregnancy, and (iii) evaluating the risk for French pregnant women. Variations of exposures due to consumption behaviors during pregnancy, and also, season of the third trimester, will be of special interest in this work.

2. Subjects and methods

2.1. The EDEN mother–child cohort study and dietary assessment

The consumption data of the EDEN mother–child cohort were used. The study design of the EDEN cohort is published elsewhere (Drouillet et al., 2009a, 2009b). Briefly, pregnant women ($n = 2002$) from 18 to 45 years old, were recruited before 24 weeks of amenorrhea, at the departments of Obstetrics and Gynecology of the University Hospitals of two French cities (Nancy and Poitiers). Enrolment for this study extended from February 2003 to January 2006.

Participants completed a food frequency questionnaire (FFQ) on their diet in the year before pregnancy and during the last three months of pregnancy. The first-trimester FFQ (completed at recruitment, on average 15 weeks of amenorrhea) concerned the usual diet during the year prior to pregnancy. The same FFQ was recompleted during the first few days following delivery, and was related to the diet during

the last three months of pregnancy. This FFQ was developed and validated in another study (Deschamps et al., 2009). Consumption frequencies were recorded for 137 different food items, with a 7-item scale from "never" to "more than once a day". For each food item, sizes of portions usually consumed by each subject were also determined using pictures for different food types (e.g. meat, French fries, pasta, vegetables, cakes, and cheese) on a 3 level scale. For the other food types, the portion consumed was assumed to be a standard portion assessed for the French adult population (Lafay et al., 2002).

Subjects for whom more than 3 food items of the FFQ were missing were excluded; median values for the sample were imputed when only one or two items were missing. Daily intake of each food item and for each subject was assessed by combining consumption frequencies and usual portion sizes recorded. Individual total energy intakes were then calculated for all subjects by multiplying the intake by the energy value of each food. Energy values were obtained from the SU.VI.MAX nutrient composition database (Herberg et al., 1994; Lemoulllec et al., 1996). Subjects with an estimated total energy intake under 1000 kcal/day or over 5000 kcal/day were excluded. At the end, 1861 FFQs were validated for the consumption in the year before pregnancy and 1775 FFQs were validated for the consumption in the last three months of pregnancy.

Individual body weight was measured using electronic Terraillon SL 351 scales (Hanson Ltd., UK) to the nearest 0.1 kg, at the different stages of the study, and 2 to 3 days after delivery.

2.2. Contamination data

Contamination data came from the second French TDS, conducted in 2006–2010 by the French Agency for Food, Environmental and Occupational Health Safety (ANSES). Details on sampling methodology of the TDS are published elsewhere (Siroit et al., 2009b).

In this study, about 20,000 food products representative of the French diet were bought in eight great regions of metropolitan France and grouped into 1319 food samples analyzed for different substances (ANSES, 2011). The samples corresponded to 212 core foods (shared out among 38 food groups), covering around 90% of the French diet (Siroit et al., 2009b). Each food was collected not only in different regions but also (when possible) during different seasons to take into account possible seasonal variation in contamination. Each sample is composed of up to 15 sub-samples of equal weight of the same food item. For each sample, 15 products were bought, prepared "as consumed" (meaning as prepared by the average consumer) and mixed together. The methods for sample analysis are described in previous publications (ANSES, 2011).

As concentration data were available for total elements only, hypotheses were used for arsenic and mercury to assess the concentrations in the different speciation forms (organic and inorganic). Level of inorganic arsenic has been assessed from level of total arsenic, by applying assumptions for inorganic arsenic proportion in the different food groups, similarly to the approach used by EFSA (EFSA, 2009). The proportions used came from scientific literature (Siroit et al., 2009a; Yost et al., 2004).

Mercury is mostly present as methylmercury (organic form of mercury) in fish and other seafood products (JECFA, 2011). Then methylmercury concentrations in fish, mollusks and crustaceans were estimated by total mercury concentrations. In other foods, the inorganic form is predominant, then inorganic mercury levels were considered equal to total mercury levels (Arnich et al., 2012).

Left-censored data, below the limit of detection (LOD) or below the limit of quantification (LOQ), were managed by two approaches. The lower-bound (LB) approach consisted in substituting the values below LOD by 0 and the values below LOQ by the LOD. The upper-bound (UB) approach consisted in replacing the values below LOD by the LOD and the values below LOQ by the LOQ.

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