Environmental contaminants and child's growth

Manik Kadawathagedara, Blandine de Lauzon-Guillain, Jérémie Botton

Environmental contaminants and child's growth

Manik Kadawathagedara[a], Blandine de Lauzon-Guillain[a], Jérémie Botton[a,b]

a. INSERM, UMR1153 Centre of Research in Epidemiology and Statistics Sorbonne Paris Cité, Team "Early Origin of the Child's Health and Development" (ORCHAD), Paris Descartes University, Paris, France

b. Univ. Paris-Sud, Université Paris-Saclay, Faculty of Pharmacy, F-92296, Châtenay-Malabry, France

Corresponding author:

Manik Kadawathagedara

Inserm UMR 1153 – Equipe Orchad

16 avenue Paul Vaillant Couturier

94807 Villejuif Cedex

manik.kadawathagedara@inserm.fr

Abstract

Experimental data have suggested that some contaminants in the environment may increase the risk of obesity. Infants can be exposed to chemicals either prenatally, by trans-placental passage of chemicals, or postnatally by their own diet and by other external pathways (air inhalation, dust, hand-to-mouth exposure) after birth. In order to provide a review of epidemiological evidence on the association between prenatal exposure to chemicals and prenatal and postnatal growth, we present the literature from systematic review articles and international meta-analyses, when available, or recent research articles when summarising articles were not available. The most studied contaminants in this field were persistent organic pollutants (e.g. organochlorinated pesticides, polychlorinated biphenyls, PCBs), non-persistent pollutants (e.g. phthalates, BPA), toxic heavy metals (i.e. cadmium, lead and mercury), arsenic, mycotoxins and acrylamide. Mounting evidence suggests that child's growth may be associated with prenatal or postnatal exposures to environmental contaminants. Improving exposure assessment and studying the contaminants as mixtures should allow to gain knowledge about the environmental determinants of growth and obesity.

Key words: chemicals, children, epidemiology, growth, review

Introduction

Infants can be exposed to chemicals either prenatally, by trans-placental passage of chemicals, or postnatally by breastfeeding, their own diet and by other external pathways (air inhalation, dust, hand-to-mouth exposure) after birth.

The placenta is the link between mothers and foetuses, and has multiple function, including transport of nutrients or oxygen and elimination of metabolic waste products. It was thought to be a barrier for drugs and chemicals but, during the last decades, evidence has accumulated that chemicals (incl. drugs) can be transferred across the placenta, by passive diffusion mechanism or active transporters (1, 2). Most of the chemicals detected in food can pass the placental barrier, and can reach the developing internal organs of the foetus, especially the brain, and some of them can accumulate.

Several pieces of evidence suggest that foetuses and infants may be more sensitive to pollutants than adults (3). First, children's metabolic pathways are immature — especially during the foetal period and the first year after birth — suggesting that metabolism and detoxification are not as efficient in infants as they are in adults. Furthermore, development processes during these periods are also more easily disturbed. Due to their higher body surface area relative to their size, even low exposure levels during this window could have detrimental effects, sometimes asymptomatic at the time of exposure but appearing later on (4).

To add some complexity to this issue, the effects of environmental contaminants on children's health can be highly dependent on exposure timing (5). Many sequential developmental processes exist in early life. The development of the foetus is unidirectional and specifically-timed. It is a complex and coordinate subsequent cellular events (6). Several studies have investigated whether the prenatal exposure to environmental contaminants can negatively affect foetal growth and a wide range of health defects. Birth weight has been extensively studied as a proxy of foetal growth and low birth weight (LBW) less than 2500g as a marker of intrauterine growth retardation (7-9).

In order to provide a summary of epidemiological evidence on the association between prenatal exposure to chemicals and prenatal and postnatal growth, we presented systematic review articles and international meta-analyses, when available, or recent research articles when summarising articles were not available. Any type of exposure assessment was selected. For postnatal growth we looked at studies using data of children under 11 years of age to avoid the potential effect of puberty. We are going to present first persistent organic pollutants, then, non-persistent pollutants (i.e. phthalates, BPA and environmental phenols), toxic heavy metals (i.e. cadmium, lead and mercury) or arsenic and, finally, other chemicals (i.e. mycotoxins and acrylamide).

Persistent organic pollutants

Persistent organic pollutants (POPs) are carbon-based chemicals. Due to their high stability they have a long half-life and are found throughout the environment. They are toxic for humans and wildlife (10). Most POPs are results of human activities, related to the use of pesticides or generated as by-products of industrial or combustion processes. Once in the environment, POPs accumulate in fatty tissue of living organisms, reaching the greatest concentrations at the top of the food chain (large fish, mammals and predatory birds). For non-accidentally and non-occupationally exposed populations, the major pathway of human exposure is from the ingestion of contaminated food. The main source (around 95%) of POPs intake is through dietary intake of animal fats (11).

We focused on exposure to POPs that have been studied in relation with child growth, namely: polychlorinated biphenyls (PCBs), polychlorinated dibenzo-p-dioxins (PCDD), polychlorinated dibenzofurans (PCDF), dichlorodiphenyl trichloroethane (DDT) and its metabolite dichlorodiphenyl dichloroethene (DDE), hexaclhorobenzene (HCB), brominated flame retardants (BFRs), perfluoroalkyl substances (PFAS).

Polychlorinated biphenyls (PCBs)

Of the 209 different types of PCBs, 13 exhibit a dioxin-like toxicity (12). Their persistence in the environment corresponds to the degree of chlorination, with higher chlorinated PCBs having longer half-lives (13). PCBs are listed as probable human carcinogens (14).

Large numbers of people have been accidentally exposed to PCBs through two cases of PCB food contamination of rice bran cooking oil during manufacture. Consumption of PCB-contaminated rice oil in Japan in 1968 and in Taiwan in 1979 caused pigmentation of nails and mucous membranes and swelling of the eyelids, along with fatigue, nausea and vomiting (15). Prenatally exposed Taiwanese children showed developmental delays and behavioural problems seven years after the accident (16). Another incidence of accidental exposure was the PCB contamination by industrial waste of the Lake Michigan in 1976. Children of mothers who consumed large amounts of contaminated fish from Lake Michigan showed poorer short-term memory function at age 4-y (17).

In non-accidentally exposed population, a large meta-analysis showed that prenatal exposure to PCB‑153 has been inversely associated with birth weight. More specifically, they reported a 150-g (95% CI: –240, –50 g) reduction per 1 μg/L increase in cord serum PCB‑153 (18). Nevertheless, prenatal exposure to PCBs does not have an established negative association with low-birth weight, defined as a newborn with birth weight less than 2,500 (19). Concerning postnatal growth, a study pooling the data of seven birth cohorts did not show any association between prenatal exposure to PCB 153 and postnatal growth from birth to 24 months, while postnatal PCB-153 was associated with decreased weight growth at European exposure levels (20).

Dioxins and Furans

Dioxins (Polychlorinated dibenzo-p-dioxins, PCDDs) and furans (Polychlorinated dibenzofurans, PCDFs) are classes of POPs and refer to a group of toxic chemical compounds that share certain physico-chemical characteristics.

Dioxins and furans have been associated with a number of adverse effects in humans (such as immune and enzyme disorders or chloracne), and are classified as possible human carcinogens (21). Diet, particularly animal products, is the major source of exposure for humans to dioxins and furans for humans. Furans persist in the environment for long periods (several days in the air), and are classified as possible human carcinogens (22). Dioxins and furans have also been detected in breast-fed infants (23).

A small meta-analysis including only two cohorts studies showed an increased risk of low birth weight after prenatal exposure to dioxins (24). A recent pooled analysis of three birth cohorts examined the effect of prenatal exposure to dioxins and dioxins like compounds and BMI at seven years in Norway, Belgium and Slovakia (25). Dioxins (PCDD, TCDD), furans (PCDF) and dioxin-like compounds (some PCBs) appeared to be associated with higher weight growth between 0 and 24 months (adjusted estimate for change in z-score: β = 0.07, 95% (confidence interval) CI: −0.01, 0.14). At 7 years, dioxins exposure was associated with a significant increase in BMI in girls but not in boys. Furthermore, girls had a 54% increased risk of being overweight at 7 years.

Dichlorodiphenyl Trichloroethane (DDT) and Dichlorodiphenyl Dichloroethene (DDE)

DDT is used to control these infectious diseases, and it is sprayed on a variety of agricultural crops, especially cotton. DDT is also applied to protect against the transmission of disease from mosquitoes, such as malaria, in several developing countries (26). Its chemical stability, its persistence (as much as 50% can remain in the soil 10-15 years after application), and its past widespread use result to present detection of DDT residues in the environment, even in remote regions of the planet, such as the Arctic (27). Although residues in domestic animals have declined steadily over the last two decades, food-borne DDT remains the greatest source of exposure for the general population. Dichlorodiphenyldichloroethene (DDE) is the primary metabolite of DDT.

The acute effects of DDT on humans are limited, but long-term exposures have been associated with chronic health effects (28). Findings regarding an association between exposure to DDT and DDE and birth weight have been inconsistent. Several studies reported a negative association between DDT levels and birth weight (29-32). On the other hand, several studies did not find any association between level of prenatal or postnatal exposure to DDT or DDE and birth weight (33-39). In the meta-analysis of 12 European birth cohorts (18), the relation between cord serum DDE and birth weight was not statistically significant. Concerning postnatal growth, Iszatt et al. showed a positive association between prenatal exposure to DDE and growth from birth to 24 month from the pooled analysis of seven European birth cohorts (20).

Hexachlorobenzene (HCB)

HCB was first introduced as a fungicide in 1945 to treat seeds and crops and was widely used to control wheat bunt. It is also a by-product of the manufacture of certain industrial chemicals and exists as an impurity in several pesticide formulations (40). The primary route of exposure to HCB for the general population is from foods such as fatty fish.

Several studies reported a negative association between HCB levels and birth weight (41-43). On the other hand, several studies did not find any association between levels of prenatal exposure to HCB and birth weight (38, 44, 45). After reviewing the literature, Tang-Peronard et al. reported an inconsistent association between HCB exposure during pregnancy and obesity risk (46). One study found that prenatal exposure to HCB increased the risk of overweight among children aged 6 years (47) and the association was stronger for children whose mothers smoked during pregnancy. Another study, showed a positive association with rapid growth in the first 6 months of life and obesity in infancy (14 months of age) (48). The prospective study of Verhulst et al., on the contrary, found no effect of prenatal exposure on growth among children aged 1 to 3 years (49). However, the small sample (n = 138) and the lack of adjustment for several potential confounders in this study may have affected the result.

Polybrominated diphenyl ethers (PBDEs)

PBDEs are a group of bromide-containing compounds. Although there are approximatively 209 PBDE congeners, only three major commercial mixtures (which contain a limited number of congeners, present in penta-, octa-, or deca-brominated forms) have been used as flame-retardants since 1965. PBDEs have very low water solubility, and when these substances are released to water, they typically bind to sediment. Humans can be exposed to PBDEs in a wide variety of ways, including consumption of contaminated foods, inhalation or skin contact (50).

A review (51) stated that there is not enough evidence to support or refute the negative relationship between PBDEs and birth weight. To date, five epidemiological studies have examined whether PBDE exposure during pregnancy affects birth weight, with 3 studies (52-54) reporting an

increased risk for low birth weight (LBW) and 2 studies (55, 56) reporting no association. The link between PBDEs and postnatal growth and obesity was classified by Vrijheid et al. as “no evidence” as only one study showed a positive association in girls, and negative in boys between maternal prenatal exposure to PBDEs and BMI at 7 years (57).

Poly- and perfluoroalkyl substances (PFAS)

PFAS, also known as perfluorinated compounds (PFCs), are a category of man-made organofluorinated compounds. Fluorocarbons are both lipophobic and hydrophobic (58). The most abundant PFAS are perfluorooctanoic acid (PFOA) and perfluorooctanesulfonic acid (PFOS), they are resistant to degradation processes, which allow them to persist in the environment (59) and have long half-lives in human body (3.8 and 5.4 years, respectively) (60). Humans are exposed to PFAS through intake of contaminated foods or through water, air and dermal exposure due to widespread use since the 1950s as surfactants and emulsifiers in consumer and industrial products. Their unique water- and oil-repelling characteristics make them suitable for diverse applications in manufacturing of food packaging and containers (eg, microwave popcorn bags) or non-stick cookware. Evidence suggests that the primary route of exposure in non-occupationally exposed populations is through the food sources (59, 61, 62). PFASs have been detected in human blood, breast milk, and cord blood.

Regarding the association between prenatal PFAS exposure and foetal growth, two recent systematic review (63, 64) found a decrease of birth weight, birth length or ponderal index for the increase in maternal serum or plasma PFOA or PFOS. One study reported a negative association between maternal PFOA or PFOS levels and postnatal growth in early infancy (5 month and 12 month, weight and BMI), (65), later results from the same study showed no association at 7 years for BMI and waist circumference (66). While, another study found a positive association between levels of prenatal exposure to PFOS and 20 month old infant weight (67).

Non persistent pollutants

Parabens, bisphenols, oxybenzone/benzophenone-3, triclosan and triclocarban are man-made chemicals used in various consumer products. Apart from triclocarban, all these compounds have a phenol group in their chemical structure and can be referred to as “environmental phenols”. Environmental phenols and phtalates are a class of chemicals that do not persist in the environment or into the body once absorbed but are also endocrine disrupting chemicals, EDCs (68). The potential influence of each category of non-persistent pollutants is described below. We have focused on the most abundant and frequently studied non-persistent pollutants: phthalates, bisphenol A and other environmental phenols.

Phthalates

Phthalates, or diesters of 1,2-benzenedicarboxylic acid (phthalic acid), are used in manufacturing of cellulose ester films, consumer articles such as toothbrushes, tool handles and toys, medical devices and drugs, ingredients in cosmetic (69, 70). Due to their widespread use, phthalates enter the environment by a variety of routes, and exposure to these compounds in industrialized countries is ubiquitous (71, 72).

Two reviews of the literature (57, 73) do not support an association of phthalates and body size at birth, mainly because of limitations and methodological differences between studies. Vrijheid et al. had classified the evidence for an effect of phthalates on foetal growth as “insufficient” (57). Some epidemiological studies showed that prenatal or childhood phthalate exposures were associated with child adiposity but, overall, the associations remain inconsistent (74). One prospective study reported negative associations between prenatal urinary concentrations of metabolites of high molecular weight phthalates and body mass index (BMI) gain during childhood in boys (75). In another study, prenatal maternal urinary concentrations of non-DEHP metabolites were negatively associated with BMI in boys at 5 years (76). In a pooled analysis of three prospective cohort studies representing 707 US children, Buckley et al. reported a sex-specific association between monoethyl phthalate (MEP) during pregnancy and BMI at 4–7 years, which was negative in

girls and positive (although not statistically significant) in boys (77). In a population of boys, maternal urinary concentrations of MEP was positively associated with weight growth velocity from two years onwards, with weight at 3 and 5 years and with BMI at five years (78). A study relying on a multi-pollutants analysis did not find any association between prenatal phthalates exposure and BMI at 7 years (79).

Bisphenol A (BPA)

Bisphenol A (BPA) is a synthetic monomer that was first developed in the 1890s and is used in many consumer products, including plastics (as a polymer, i.e. polycarbonate plastic), polyvinyl chloride (PVC), food packaging, dental sealants, and thermal receipts (80, 81). Humans are exposed to BPA through their diet, inhalation of household dust, and dermal exposure (82, 83).

A review (84) showed that the evidence of BPA affecting birth weight is equivocal. The authors stated that the literature does not support a clear link between prenatal BPA exposure and altered birth weight in the offspring and conclude that more studies, examining exposures at several time points during gestation, are needed. Snijder et al. showed in their study, where maternal urinary BPA levels were assessed, that the negative association between BPA and foetal growth was sensitive to the numbers of BPA measurements (85). Another review had classified the evidence for an effect of BPA on foetal growth as “insufficient” (57). The epidemiological studies on the relationship between BPA and overweight or obesity in children are also inconclusive. Results from cross-sectional studies mainly show that higher urinary BPA concentrations are positively associated with obesity (86-89), but the direction of the relationship cannot be established using such a design. Few prospective cohort studies examined early-life BPA exposure in association with later childhood BMI (68, 90-93). One study found that higher prenatal BPA exposure was associated with higher BMI or weight-for-height among children (68, 93), another study did not found any association between prenatal BPA with postnatal growth (Philippat et al., 2014), while one other reported higher exposure in early childhood was related with lower BMI later in childhood (90). The most recent study found that higher BPA concentrations in children's urine at 4 years of age were associated with

higher BMI z-score, whereas prenatal urinary BPA concentrations were negatively associated with BMI and adiposity measures in girls and positively in boys (92).

Other Environmental Phenols

Commonly studied environmental phenols, other than BPA, include parabens, oxybenzone/benzophenone-3 (OXBE), triclosan (TRCS) and triclocarban (TRCB). Parabens are alkyl or aryl esters of para-hydroxy benzoic acid (PHBA) and have mainly been used as antimicrobial preservatives in food, personal care products and pharmaceuticals (94). OXBE is mainly used as UV filters in sunscreens and as UV stabilizer in some food packaging (95). TRCS and TRCB are used as antimicrobial and antifungal agent in products like toothpaste, soaps, detergents and other hygiene and PCPs (96). Although these environmental phenols are non-persistent chemicals and have short elimination half-lives in humans (parabens: 1-7 hours, OXBE: < 24 hours (97) and TRCS: 2 days (98)), their widespread use and potential endocrine disrupting properties have made them chemicals of concern (99, 100).

Environmental phenols can be found in air and water after release from the manufacture, use, and disposal of products containing these compounds. In soil, they are likely to move to groundwater. Low levels of phenol have been found in foods such as smoked summer sausage, smoked pork belly, mountain cheese, fried bacon, fried chicken, and black fermented tea (101).

Evidence concerning the effect of phenol exposure on a lower size at birth is limited (8). In the French EDEN mother-child cohort, exposure to these chemicals and pre and post-natal growth has been studied. Triclosan concentration in maternal mid-pregnancy urine sample was negatively associated with growth parameters measured at the third ultrasound examination but not earlier in pregnancy (68). At birth, this phenol exposure tended to be negatively associated with head circumference but not with weight or height. Parabens concentration in maternal mid-pregnancy urine was positively associated with weight at birth. This positive association remained until 3 years for methylparaben.

Toxic heavy metals

Toxic heavy metals, such as cadmium, lead, arsenic and mercury, are a group of toxic compounds among which endocrine disrupting activities have been described for some, but not all, of them. They are ubiquitous environmental pollutants. The most common sources of exposure for the general population are through air inhalation and dietary intake. Exposure to heavy metals can occur through inhalation of contaminated air. Air contamination occurs through gasoline and coal combustion, industrial emissions, and the spraying of metal-based pesticides.

Cadmium (Cd)

Cadmium is a heavy metal which occurs both naturally and as a pollutant associated with many modern industrial processes throughout the world. In the general population, the main exposure sources of cadmium are smoking, due to high cadmium content in tobacco leaves, and cadmium-contaminated foods resulting from production in contaminated soil (102). Cadmium is known to have endocrine disrupting activities (8) and is also a human carcinogen, classified as group I by the IARC (103).

Lead (Pb)

Lead occurs naturally in the environment. However, most of the high levels found throughout the environment come from human activities (104). Pb is a highly toxic compound to the human body. Since the earliest recorded times, lead has been widely used in human life. The metal has been smelted, applied as a cosmetic, painted on buildings, and glazed on ceramic pots. On the other hand, lead may be the oldest recognized chemical toxin (105).

Arsenic (As)

Arsenic is a naturally occurring element that is widely distributed in the Earth's crust and exists in several forms. Arsenic combined with oxygen, chlorine or sulfur is called inorganic As. When combined with carbon and hydrogen is referred to organic arsenic (106). Arsenic is a potent toxicant and carcinogen (107). Drinking water is one of the major sources of As exposure in some parts of the world and it is present in a wide variety of foods including fish and rice (108).

Mercury (Hg)

Mercury occurs naturally in the environment and exists in several forms. These forms can be organized under three headings: metallic mercury (also known as elemental mercury), inorganic mercury, and organic mercury (109). Hg is formed mainly by bacterial methylation of inorganic mercury (IHg) into the organic form methylmercury (MeHg). This transformation occurs in aquatic sediments with bioaccumulation in the food web. Fish and other seafood contain the highest concentrations of Hg, with only small amounts in other food groups (110).

A number of studies have reported a negative association between in utero lead exposure and birth weight, but the literature is more limited for the other metals (8). Nevertheless, a recent review (57) including prospective studies and meta-analysis published after the 1st of September 2015, reported for prenatal growth a negative association between heavy metals (lead, mercury, cadmium) and arsenic and had classified the evidence as “moderate”. Concerning postnatal growth, ten studies on prenatal or postnatal exposure to heavy metals (cadmium, arsenic, mercury or lead) showed negative associations with postnatal growth in children but, due to a limited number of studies per specific heavy metals, authors classified evidence as “insufficient” (57). A recent cross-sectional study in homeless children aged under 6 years did not show strong evidence for negative association between metals (lead, mercury, cadmium) or arsenic and weight or height, although some negative trends between As or Cd and height were observed (111) .

Others chemicals

Mycotoxins

A mycotoxin is a toxic metabolite produced by fungi colonizing crops (112). One of the most studied mycotoxin is aflatoxin, known to be a human carcinogens (113). Milk and dairy products are the most important food sources of aflatoxin. Zearalenone is another type of mycotoxin, present in grains and other plant foods through fungal contamination by Fusarium species (112), and in animal products (e.g., meat, eggs, and dairy products) through deliberate introduction of zeranol into livestock to promote growth and improve beef/meat production. Zeranol is a synthetic derivate of

zearalenone. Finally, trichothecene mycotoxin deoxynivalenol (DON) is a mycotoxin produced in wheat, barley and corn following infestation by Fusarium species in the weld and during storage (112).

A review reported six studies with significant associations or correlations between low birth weight and aflatoxin while one study did not find any correlation (114). In a longitudinal study of 138 Gambian infants, exposure to aflatoxin during pregnancy was inversely associated with height-for-age and weight-for-age Z-score in the first year of life (115). Another longitudinal study of 200 infants from Benin showed a negative association between aflatoxin-albumin adducts in infants blood at recruitment, and height-for-age Z-score and weight-for-height Z-score 4 to 8 months later (116).

To our knowledge no epidemiological study has investigated the association between zearalenone and prenatal growth. In a case-control study of girls, where cases had precocious puberty, no significant correlation between urinary zearalenone levels and BMI was found in any group (117). Another cross sectional study showed that girls with detectable urinary zearalenone levels tended to be shorter (118).

Experimental animal studies on DON's chronic toxic effects indicated that growth was the parameter most likely to be affected by DON (119). To our knowledge no previous epidemiological study has linked the effect of DON exposure to prenatal or postnatal growth (120, 121).

Acrylamide

Acrylamide is a colourless, odourless, low molecular weight, highly water-soluble organic compound. It is a known neurotoxic for humans and animals and was classified as probably carcinogenic in humans (group 2A) by the International Agency for Research on Cancer (122). It is a chemical arising in a wide variety of carbohydrate-containing foods during frying or baking at high temperatures.

Three longitudinal studies have shown a relationship between higher maternal acrylamide exposure and lower birth weight or higher risk of having a SGA baby (123, 124). To our knowledge one study showed a positive association between acrylamide exposure and postnatal growth (125).

The literature evidence on prenatal exposure to environmental contaminants and pre or post-natal growth presented was summarized in **Table 1**.

Table 1*: Summary of the literature on prenatal exposure to environmental contaminant's and child growth*

Potential mechanisms

Epigenetic modifications

In studies related to the DOHaD hypothesis, the epigenetic modifications due to adverse environmental exposure are often cited as a possible mechanism (126). These modifications could induce heritable and persistent changes in gene expression without altering the DNA sequence. The three major molecular substrates that are involved in this process are the DNA, proteins that form the core around which the DNA wraps (histones) and a specific form of RNA molecules (noncoding RNA). Epigenetic changes include DNA methylation, chromatin folding or binding and packaging of DNA around nucleosomes and, finally, covalent modifications of the histone proteins (126). A recent review found that in the context of child health, the impact of environmental modification on the epigenome are of small magnitude. However, these small environmental effects (maternal smoking, exposure to heavy metals or phthalates and phenols) on the epigenome have been replicated across populations and across time. Therefore, the authors conclude about the need of having critical discourse on findings such small effects. Meanwhile, they advocate the research to emphasis the studies on the dynamic nature of the epigenome with the help of longitudinal studies (127).

Endocrine disrupting chemicals (EDCs)

According to World Health Organization (WHO) (128), "An endocrine disruptor is an exogenous substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub) populations". They can mimic or interfere with the effects of endogenous hormones (129). EDCs can potentially affect all the human hormonal systems ranging from metabolism to growth, neurodevelopment or reproduction (128,

130, 131). Many studies are suggesting that these chemicals could have an obesogenic effect, known as the "environmental obesogenic hypothesis" (20, 92, 93). In the increase of obesity prevalence, EDCs might play a role beyond traditional risk factors (46, 132). Because by definition they interfere with hormonal actions, sex-specific effects are expected for many EDCs (133). Moreover, the fetal and early postnatal periods would be of high susceptibility to these environmental exposures (134, 135).

Oxidative stress

Another possible biological pathway between exposure to environmental contaminants and growth is through oxidative stress. Oxidative stress is an imbalance between the production and elimination of reactive species that leads to damages in macromolecules. The principal reactive species are reactive oxygen species (ROS) and nitrogen oxygen species (RNS). Most environnemental contaminants induce abnormal ROS generation (136). Oxidative stress seems to be implicated in suboptimal fetal conditions, due to poor intrauterine environment and alterations of physiologic systems of cardiovascular control (e.g. renin-angiotensin-aldosterone system, hypothalamic-pituitary-adrenal axis) (136)."

Conclusion

Environment factors can affect the development of the foetus. For instance, a widely studied exposure as exposures to tobacco smoke during pregnancy was well documented in association with child's growth (137). Mounting evidence suggests that child's growth may also be influenced by prenatal or postnatal exposures to some environmental contaminants (e.g. PCBs, DDE) but, for other chemicals than tobacco, the literature is sparse and characterised by large inconsistencies.

To gain knowledge about these associations, research in epidemiology should focus mainly on improving exposure assessment. The use of biomarkers is widespread in environmental studies, but the use of these data has important limitation. For example, when assaying non-persistent chemicals (phthalates, BPA), the characterisation of the exposure is difficult due to short half-life for some chemicals and high within-subject variability. On the contrary, POPs or for some metals that

have long half-lives (up to years) and the use of biomarker measurement can give a good estimate of long-term past exposure. Moreover, studying the contaminants as mixtures and not individually could be interesting to deal with the exposures to many individual contaminants at low doses, some sharing similar mechanisms and routes of exposure (e.g. diet, or tobacco smoke). In fact, exposures may be highly correlated, within and between the different chemical classes (e.g. PCBs, PBDEs, PFASs, and phthalates) (Robinson et al., 2015) (138) and it can be challenging to identify the chemicals responsible for growth impairment.

Finally, we also need to pay attention about considering growth as a whole, reporting the associations at least with height, weight and weight-for-height as well.

To conclude, only limited associations were reviewed here between exposure to environmental contaminants and child's prenatal or postnatal growth. New-borns, infants and children need to be considered as sensitive populations and policies aiming to reduce the exposure of this population are needed.

Acknowledgement: none

Financial support

This research was supported by Agence Nationale de la Recherche (ANR) (Grant number ANR-14-CE21-0002). Support for M.K. was provided by a doctoral grant from CORDDIM (field of major interest of the Île-de-France Regional Council "Cardiovascular/Obesity/Kidney/Diabetes").

Conflicts of Interest: none

References

1. Giaginis C, Theocharis S, Tsantili-Kakoulidou A. Current toxicological aspects on drug and chemical transport and metabolism across the human placental barrier. Expert Opin Drug Metab Toxicol 2012;8(10):1263-75. doi: 10.1517/17425255.2012.699041.

2. Myren M, Mose T, Mathiesen L, Knudsen LE. The human placenta--an alternative for studying foetal exposure. Toxicology in vitro : an international journal published in association with BIBRA 2007;21(7):1332-40. doi: 10.1016/j.tiv.2007.05.011.
3. Landrigan P, Garg A, Droller DB. Assessing the effects of endocrine disruptors in the National Children's Study. Environ Health Perspect 2003;111(13):1678-82.
4. Barouki R, Gluckman PD, Grandjean P, Hanson M, Heindel JJ. Developmental origins of non-communicable disease: implications for research and public health. Environ Health 2012;11:42. doi: 10.1186/1476-069X-11-42.
5. Liu SH, Bobb JF, Lee KH, et al. Lagged kernel machine regression for identifying time windows of susceptibility to exposures of complex mixtures. Biostatistics 2017. doi: 10.1093/biostatistics/kxx036.
6. Nowakowski RS, Hayes NL. CNS development: an overview. Dev Psychopathol 1999;11(3):395-417.
7. Schoeters GE, Den Hond E, Koppen G, et al. Biomonitoring and biomarkers to unravel the risks from prenatal environmental exposures for later health outcomes. Am J Clin Nutr 2011;94(6 Suppl):1964S-9S. doi: 10.3945/ajcn.110.001545.
8. Slama R, Cordier S. [Impact of chemical and physical environmental factors on the course and outcome of pregnancy]. Journal de gynecologie, obstetrique et biologie de la reproduction 2013;42(5):413-44. doi: 10.1016/j.jgyn.2013.02.012.
9. Wigle DT, Arbuckle TE, Turner MC, et al. Epidemiologic evidence of relationships between reproductive and child health outcomes and environmental chemical contaminants. Journal of toxicology and environmental health Part B, Critical reviews 2008;11(5-6):373-517. doi: 10.1080/10937400801921320.
10. Stockholm Convention. Stockholm Convention on persistent organic polluants. 2001.
11. Magliano DJ, Loh VH, Harding JL, Botton J, Shaw JE. Persistent organic pollutants and diabetes: a review of the epidemiological evidence. Diabetes Metab 2014;40(1):1-14. doi: 10.1016/j.diabet.2013.09.006.
12. Giesy JP, Kannan K. Dioxin-like and non-dioxin-like toxic effects of polychlorinated biphenyls (PCBs): implications for risk assessment. Crit Rev Toxicol 1998;28(6):511-69. doi: 10.1080/10408449891344263.
13. Agency for Toxic Substances and Disease Registry. Toxicological profile for Polychorinated biphenyls (PCBs). Atlanta, US: Public Health Service, 2000.
14. IARC. IARC Monogrpahs on the evaluation of carcinogenic risks to humans: Polychlorinated biphenyls and polybrominated biphenyls Lyon, France, 2016.
15. Lu YC, Wong PN. PCB poisoning in Japan and Taiwan. Dermatological, medical, and laboratory findings of patients in Taiwan and their treatments. Prog Clin Biol Res 1984;137:81-115.
16. Chen YC, Yu ML, Rogan WJ, Gladen BC, Hsu CC. A 6-year follow-up of behavior and activity disorders in the Taiwan Yu-cheng children. American journal of public health 1994;84(3):415-21.
17. Jacobson JL, Jacobson SW, Humphrey HE. Effects of in utero exposure to polychlorinated biphenyls and related contaminants on cognitive functioning in young children. The Journal of pediatrics 1990;116(1):38-45.
18. Govarts E, Nieuwenhuijsen M, Schoeters G, et al. Birth weight and prenatal exposure to polychlorinated biphenyls (PCBs) and dichlorodiphenyldichloroethylene (DDE): a meta-analysis within 12 European Birth Cohorts. Environ Health Perspect 2012;120(2):162-70. doi: 10.1289/ehp.1103767.
19. El Majidi N, Bouchard M, Gosselin NH, Carrier G. Relationship between prenatal exposure to polychlorinated biphenyls and birth weight: a systematic analysis of published epidemiological studies through a standardization of biomonitoring data. Regulatory toxicology and pharmacology : RTP 2012;64(1):161-76. doi: 10.1016/j.yrtph.2012.06.007.

20. Iszatt N, Stigum H, Verner MA, et al. Prenatal and Postnatal Exposure to Persistent Organic Pollutants and Infant Growth: A Pooled Analysis of Seven European Birth Cohorts. Environ Health Perspect 2015;123(7):730-6. doi: 10.1289/ehp.1308005.
21. IARC. IARC Monographs on the evaluation of carcinogenic risks to humans: 2,3,7,8-TCDD, 2,3,4,7,8-PeCDF, PCB 126. Lyon, France, 1987.
22. IARC. IARC Monographs on the evaluation of carcinogenic risks to humans: Furan. Lyon, 1995.
23. Leung HW, Kerger BD, Paustenbach DJ. Elimination half-lives of selected polychlorinated dibenzodioxins and dibenzofurans in breast-fed human infants. J Toxicol Environ Health A 2006;69(6):437-43. doi: 10.1080/15287390500246886.
24. Pan X, Liu X, Li X, et al. Association between Environmental Dioxin-Related Toxicants Exposure and Adverse Pregnancy Outcome: Systematic Review and Meta-Analysis. Int J Fertil Steril 2015;8(4):351-66.
25. Iszatt N, Stigum H, Govarts E, et al. Perinatal exposure to dioxins and dioxin-like compounds and infant growth and body mass index at seven years: A pooled analysis of three European birth cohorts. Environ Int 2016;94:399-407. doi: 10.1016/j.envint.2016.04.040.
26. Agency for Toxic Substances and Disease Registry. Toxicological Profile for DDT, DDE, and DDD. Atlanta, US: Public Health Service 2002.
27. AMAP AMaAPA. AMAP assessment 2009: Human Health in the Artic. Oslo, 2009.
28. ATSDR. Toxicological Profile for DDT, DDE, and DDD. Atlanta, US: Public Health Service 2002.
29. Longnecker MP, Klebanoff MA, Zhou H, Brock JW. Association between maternal serum concentration of the DDT metabolite DDE and preterm and small-for-gestational-age babies at birth. Lancet 2001;358(9276):110-4. doi: 10.1016/S0140-6736(01)05329-6.
30. Rogan WJ, Gladen BC, McKinney JD, et al. Polychlorinated biphenyls (PCBs) and dichlorodiphenyl dichloroethene (DDE) in human milk: effects of maternal factors and previous lactation. American journal of public health 1986;76(2):172-7.
31. Siddiqui MK, Srivastava S, Srivastava SP, Mehrotra PK, Mathur N, Tandon I. Persistent chlorinated pesticides and intra-uterine foetal growth retardation: a possible association. Int Arch Occup Environ Health 2003;76(1):75-80. doi: 10.1007/s00420-002-0393-6.
32. Weisskopf MG, Anderson HA, Hanrahan LP, et al. Maternal exposure to Great Lakes sport-caught fish and dichlorodiphenyl dichloroethylene, but not polychlorinated biphenyls, is associated with reduced birth weight. Environ Res 2005;97(2):149-62. doi: 10.1016/j.envres.2004.01.014.
33. Bjerregaard P, Hansen JC. Organochlorines and heavy metals in pregnant women from the Disko Bay area in Greenland. The Science of the total environment 2000;245(1-3):195-202.
34. Dewailly E, Ayotte P, Bruneau S, Laliberte C, Muir DC, Norstrom RJ. Inuit exposure to organochlorines through the aquatic food chain in arctic quebec. Environ Health Perspect 1993;101(7):618-20.
35. Farhang L, Weintraub JM, Petreas M, Eskenazi B, Bhatia R. Association of DDT and DDE with birth weight and length of gestation in the Child Health and Development Studies, 1959-1967. Am J Epidemiol 2005;162(8):717-25. doi: 10.1093/aje/kwi276.
36. Gladen BC, Shkiryak-Nyzhnyk ZA, Chyslovska N, Zadorozhnaja TD, Little RE. Persistent organochlorine compounds and birth weight. Annals of epidemiology 2003;13(3):151-7.
37. Karmaus W, Zhu X. Maternal concentration of polychlorinated biphenyls and dichlorodiphenyl dichlorethylene and birth weight in Michigan fish eaters: a cohort study. Environ Health 2004;3(1):1. doi: 10.1186/1476-069X-3-1.
38. Ribas-Fito N, Sala M, Cardo E, et al. Association of hexachlorobenzene and other organochlorine compounds with anthropometric measures at birth. Pediatr Res 2002;52(2):163-7. doi: 10.1203/00006450-200208000-00006.
39. Rogan WJ, Gladen BC, McKinney JD, et al. Neonatal effects of transplacental exposure to PCBs and DDE. The Journal of pediatrics 1986;109(2):335-41.

40. Agency for Toxic Substances and Disease Registry. Toxicological Profile for Hexachlorobenzene. Atlanta, US: Public Health Service, 2015.
41. Guo H, Jin Y, Cheng Y, et al. Prenatal exposure to organochlorine pesticides and infant birth weight in China. Chemosphere 2014;110:1-7. doi: 10.1016/j.chemosphere.2014.02.017.
42. Lopez-Espinosa MJ, Murcia M, Iniguez C, et al. Prenatal exposure to organochlorine compounds and birth size. Pediatrics 2011;128(1):e127-34. doi: 10.1542/peds.2010-1951.
43. Vafeiadi M, Vrijheid M, Fthenou E, et al. Persistent organic pollutants exposure during pregnancy, maternal gestational weight gain, and birth outcomes in the mother-child cohort in Crete, Greece (RHEA study). Environ Int 2014;64:116-23. doi: 10.1016/j.envint.2013.12.015.
44. Fenster L, Eskenazi B, Anderson M, et al. Association of in utero organochlorine pesticide exposure and fetal growth and length of gestation in an agricultural population. Environ Health Perspect 2006;114(4):597-602.
45. Sagiv SK, Tolbert PE, Altshul LM, Korrick SA. Organochlorine exposures during pregnancy and infant size at birth. Epidemiology 2007;18(1):120-9. doi: 10.1097/01.ede.0000249769.15001.7c.
46. Tang-Peronard JL, Andersen HR, Jensen TK, Heitmann BL. Endocrine-disrupting chemicals and obesity development in humans: a review. Obesity reviews : an official journal of the International Association for the Study of Obesity 2011;12(8):622-36. doi: 10.1111/j.1467-789X.2011.00871.x.
47. Smink A, Ribas-Fito N, Garcia R, et al. Exposure to hexachlorobenzene during pregnancy increases the risk of overweight in children aged 6 years. Acta paediatrica 2008;97(10):1465-9. doi: 10.1111/j.1651-2227.2008.00937.x.
48. Valvi D, Mendez MA, Garcia-Esteban R, et al. Prenatal exposure to persistent organic pollutants and rapid weight gain and overweight in infancy. Obesity (Silver Spring) 2014;22(2):488-96. doi: 10.1002/oby.20603.
49. Verhulst SL, Nelen V, Hond ED, et al. Intrauterine exposure to environmental pollutants and body mass index during the first 3 years of life. Environ Health Perspect 2009;117(1):122-6. doi: 10.1289/ehp.0800003.
50. Agency for Toxic Substances and Disease Registry. Toxicological profile for Polubrominated Diphenyl Ethers (PBDEs). Atlanta, US: Public Health Service, 2017.
51. Zheng T, Zhang J, Sommer K, et al. Effects of Environmental Exposures on Fetal and Childhood Growth Trajectories. Ann Glob Health 2016;82(1):41-99. doi: 10.1016/j.aogh.2016.01.008.
52. Chao HR, Wang SL, Lee WJ, Wang YF, Papke O. Levels of polybrominated diphenyl ethers (PBDEs) in breast milk from central Taiwan and their relation to infant birth outcome and maternal menstruation effects. Environ Int 2007;33(2):239-45. doi: 10.1016/j.envint.2006.09.013.
53. Harley KG, Chevrier J, Aguilar Schall R, Sjodin A, Bradman A, Eskenazi B. Association of prenatal exposure to polybrominated diphenyl ethers and infant birth weight. Am J Epidemiol 2011;174(8):885-92. doi: 10.1093/aje/kwr212.
54. Wu K, Xu X, Liu J, Guo Y, Li Y, Huo X. Polybrominated diphenyl ethers in umbilical cord blood and relevant factors in neonates from Guiyu, China. Environmental science & technology 2010;44(2):813-9. doi: 10.1021/es9024518.
55. Mazdai A, Dodder NG, Abernathy MP, Hites RA, Bigsby RM. Polybrominated diphenyl ethers in maternal and fetal blood samples. Environ Health Perspect 2003;111(9):1249-52.
56. Tan J, Loganath A, Chong YS, Obbard JP. Exposure to persistent organic pollutants in utero and related maternal characteristics on birth outcomes: a multivariate data analysis approach. Chemosphere 2009;74(3):428-33. doi: 10.1016/j.chemosphere.2008.09.045.
57. Vrijheid M, Casas M, Gascon M, Valvi D, Nieuwenhuijsen M. Environmental pollutants and child health-A review of recent concerns. Int J Hyg Environ Health 2016;219(4-5):331-42. doi: 10.1016/j.ijheh.2016.05.001.

58. Agency for Toxic Substances and Disease Registry. Draft, Toxicological profile perfluoroalkyls. Atlanta, Us: Public Health Service, 2015.
59. Lindstrom AB, Strynar MJ, Libelo EL. Polyfluorinated compounds: past, present, and future. Environmental science & technology 2011;45(19):7954-61. doi: 10.1021/es2011622.
60. Olsen GW, Burris JM, Ehresman DJ, et al. Half-life of serum elimination of perfluorooctanesulfonate,perfluorohexanesulfonate, and perfluorooctanoate in retired fluorochemical production workers. Environ Health Perspect 2007;115(9):1298-305. doi: 10.1289/ehp.10009.
61. Fromme H, Tittlemier SA, Volkel W, Wilhelm M, Twardella D. Perfluorinated compounds--exposure assessment for the general population in Western countries. Int J Hyg Environ Health 2009;212(3):239-70. doi: 10.1016/j.ijheh.2008.04.007.
62. Haug LS, Huber S, Becher G, Thomsen C. Characterisation of human exposure pathways to perfluorinated compounds--comparing exposure estimates with biomarkers of exposure. Environ Int 2011;37(4):687-93. doi: 10.1016/j.envint.2011.01.011.
63. Bach CC, Bech BH, Brix N, Nohr EA, Bonde JP, Henriksen TB. Perfluoroalkyl and polyfluoroalkyl substances and human fetal growth: a systematic review. Crit Rev Toxicol 2015;45(1):53-67. doi: 10.3109/10408444.2014.952400.
64. Johnson PI, Sutton P, Atchley DS, et al. The Navigation Guide - evidence-based medicine meets environmental health: systematic review of human evidence for PFOA effects on fetal growth. Environ Health Perspect 2014;122(10):1028-39. doi: 10.1289/ehp.1307893.
65. Andersen CS, Fei C, Gamborg M, Nohr EA, Sorensen TI, Olsen J. Prenatal exposures to perfluorinated chemicals and anthropometric measures in infancy. Am J Epidemiol 2010;172(11):1230-7. doi: 10.1093/aje/kwq289.
66. Andersen CS, Fei C, Gamborg M, Nohr EA, Sorensen TI, Olsen J. Prenatal exposures to perfluorinated chemicals and anthropometry at 7 years of age. Am J Epidemiol 2013;178(6):921-7. doi: 10.1093/aje/kwt057.
67. Maisonet M, Terrell ML, McGeehin MA, et al. Maternal concentrations of polyfluoroalkyl compounds during pregnancy and fetal and postnatal growth in British girls. Environ Health Perspect 2012;120(10):1432-7. doi: 10.1289/ehp.1003096.
68. Philippat C, Botton J, Calafat AM, Ye X, Charles MA, Slama R. Prenatal exposure to phenols and growth in boys. Epidemiology 2014;25(5):625-35. doi: 10.1097/ede.0000000000000132.
69. Agency for Toxic Substances and Disease Registry. Toxicological profile for Di(2-ethylhexyl)phthalate (DEHP). Atlanta, US: Public Health Service, 2002.
70. Hauser R, Duty S, Godfrey-Bailey L, Calafat AM. Medications as a source of human exposure to phthalates. Environ Health Perspect 2004;112(6):751-3.
71. ATSDR. Toxicological profile for Di(2-ethylhexyl)phthalate (DEHP). Atlanta, US: Public Health Service, 2002.
72. Blount BC, Silva MJ, Caudill SP, et al. Levels of seven urinary phthalate metabolites in a human reference population. Environ Health Perspect 2000;108(10):979-82.
73. Marie C, Vendittelli F, Sauvant-Rochat MP. Obstetrical outcomes and biomarkers to assess exposure to phthalates: A review. Environ Int 2015;83:116-36. doi: 10.1016/j.envint.2015.06.003.
74. Braun JM. Early-life exposure to EDCs: role in childhood obesity and neurodevelopment. Nat Rev Endocrinol 2017;13(3):161-73. doi: 10.1038/nrendo.2016.186.
75. Valvi D, Casas M, Romaguera D, et al. Prenatal Phthalate Exposure and Childhood Growth and Blood Pressure: Evidence from the Spanish INMA-Sabadell Birth Cohort Study. Environ Health Perspect 2015;123(10):1022-9. doi: 10.1289/ehp.1408887.
76. Maresca MM, Hoepner LA, Hassoun A, et al. Prenatal Exposure to Phthalates and Childhood Body Size in an Urban Cohort. Environ Health Perspect 2016;124(4):514-20. doi: 10.1289/ehp.1408750.

77. Buckley JP, Engel SM, Braun JM, et al. Prenatal Phthalate Exposures and Body Mass Index Among 4- to 7-Year-old Children: A Pooled Analysis. Epidemiology 2016;27(3):449-58. doi: 10.1097/EDE.0000000000000436.
78. Botton J, Philippat C, Calafat AM, et al. Phthalate pregnancy exposure and male offspring growth from the intra-uterine period to five years of age. Environ Res 2016;151:601-9. doi: 10.1016/j.envres.2016.08.033.
79. Agay-Shay K, Martinez D, Valvi D, et al. Exposure to Endocrine-Disrupting Chemicals during Pregnancy and Weight at 7 Years of Age: A Multi-pollutant Approach. Environ Health Perspect 2015;123(10):1030-7. doi: 10.1289/ehp.1409049.
80. Le HH, Carlson EM, Chua JP, Belcher SM. Bisphenol A is released from polycarbonate drinking bottles and mimics the neurotoxic actions of estrogen in developing cerebellar neurons. Toxicol Lett 2008;176(2):149-56. doi: 10.1016/j.toxlet.2007.11.001.
81. Munguia-Lopez EM, Gerardo-Lugo S, Peralta E, Bolumen S, Soto-Valdez H. Migration of bisphenol A (BPA) from can coatings into a fatty-food simulant and tuna fish. Food additives and contaminants 2005;22(9):892-8. doi: 10.1080/02652030500163674.
82. Geens T, Aerts D, Berthot C, et al. A review of dietary and non-dietary exposure to bisphenol-A. Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association 2012;50(10):3725-40. doi: 10.1016/j.fct.2012.07.059.
83. Vandenberg LN, Hauser R, Marcus M, Olea N, Welshons WV. Human exposure to bisphenol A (BPA). Reprod Toxicol 2007;24(2):139-77. doi: 10.1016/j.reprotox.2007.07.010.
84. Rochester JR. Bisphenol A and human health: a review of the literature. Reprod Toxicol 2013;42:132-55. doi: 10.1016/j.reprotox.2013.08.008.
85. Snijder CA, Heederik D, Pierik FH, et al. Fetal growth and prenatal exposure to bisphenol A: the generation R study. Environ Health Perspect 2013;121(3):393-8. doi: 10.1289/ehp.1205296.
86. Bhandari R, Xiao J, Shankar A. Urinary bisphenol A and obesity in U.S. children. Am J Epidemiol 2013;177(11):1263-70. doi: 10.1093/aje/kws391.
87. Eng DS, Lee JM, Gebremariam A, Meeker JD, Peterson K, Padmanabhan V. Bisphenol A and chronic disease risk factors in US children. Pediatrics 2013;132(3):e637-45. doi: 10.1542/peds.2013-0106.
88. Trasande L, Attina TM, Blustein J. Association between urinary bisphenol A concentration and obesity prevalence in children and adolescents. Jama 2012;308(11):1113-21. doi: 10.1001/2012.jama.11461.
89. Wang HX, Zhou Y, Tang CX, Wu JG, Chen Y, Jiang QW. Association between bisphenol A exposure and body mass index in Chinese school children: a cross-sectional study. Environ Health 2012;11:79. doi: 10.1186/1476-069x-11-79.
90. Braun JM, Lanphear BP, Calafat AM, et al. Early-life bisphenol a exposure and child body mass index: a prospective cohort study. Environ Health Perspect 2014;122(11):1239-45. doi: 10.1289/ehp.1408258.
91. Harley KG, Aguilar Schall R, Chevrier J, et al. Prenatal and postnatal bisphenol A exposure and body mass index in childhood in the CHAMACOS cohort. Environ Health Perspect 2013;121(4):514-20. doi: 10.1289/ehp.1205548.
92. Vafeiadi M, Roumeliotaki T, Myridakis A, et al. Association of early life exposure to bisphenol A with obesity and cardiometabolic traits in childhood. Environ Res 2016;146:379-87. doi: 10.1016/j.envres.2016.01.017.
93. Valvi D, Casas M, Mendez MA, et al. Prenatal bisphenol a urine concentrations and early rapid growth and overweight risk in the offspring. Epidemiology 2013;24(6):791-9. doi: 10.1097/EDE.0b013e3182a67822.
94. Boberg J, Taxvig C, Christiansen S, Hass U. Possible endocrine disrupting effects of parabens and their metabolites. Reprod Toxicol 2010;30(2):301-12. doi: 10.1016/j.reprotox.2010.03.011.

95. Krause M, Klit A, Blomberg Jensen M, et al. Sunscreens: are they beneficial for health? An overview of endocrine disrupting properties of UV-filters. Int J Androl 2012;35(3):424-36. doi: 10.1111/j.1365-2605.2012.01280.x.
96. Witorsch RJ, Thomas JA. Personal care products and endocrine disruption: A critical review of the literature. Crit Rev Toxicol 2010;40 Suppl 3:1-30. doi: 10.3109/10408444.2010.515563.
97. Kim S, Choi K. Occurrences, toxicities, and ecological risks of benzophenone-3, a common component of organic sunscreen products: a mini-review. Environ Int 2014;70:143-57. doi: 10.1016/j.envint.2014.05.015.
98. Sandborgh-Englund G, Adolfsson-Erici M, Odham G, Ekstrand J. Pharmacokinetics of triclosan following oral ingestion in humans. J Toxicol Environ Health A 2006;69(20):1861-73. doi: 10.1080/15287390600631706.
99. Bergman Å, Heindel JJ, Jobling S, Kidd KA, Zoeller RT. State of the science of endocrine disrupting chemicals 2012. 2013.
100. Ghazipura M, McGowan R, Arslan A, Hossain T. Exposure to benzophenone-3 and reproductive toxicity: A systematic review of human and animal studies. Reprod Toxicol 2017;73:175-83. doi: 10.1016/j.reprotox.2017.08.015.
101. Agency for Toxic Substances and Disease Registry. Toxicological Profile for Phenol. Atlanta,US: Public Health Service 2008.
102. Agency for Toxic Substances and Disease Registry. Toxicological Profile for Cadmium. Atlanta, US: Public Health Service, 2012.
103. IARC. IARC Monogrpahs on the evaluation of carcinogenic risks to humans: Cadmium and cadmium compounds. Lyon, France, 2012.
104. Agency for Toxic Substances and Disease Registry. Toxicological Profile for Lead. Atlanta, US: Public Health Service, 2007.
105. Chisolm JJ, Jr. Ancient sources of lead and lead poisoning in the United States today. West J Med 1985;143(3):380-1.
106. Agency for Toxic Substances and Disease Registry. Toxicological Profile for Arsenic. Atlanta, US: Public Health Service, 2007.
107. IARC. IARC Monographs on the evaluation of carcinogenic risks to humans: Arsenic and Arsenic compounds. Lyon, France, 2012.
108. Carlin DJ, Naujokas MF, Bradham KD, et al. Arsenic and Environmental Health: State of the Science and Future Research Opportunities. Environ Health Perspect 2016;124(7):890-9. doi: 10.1289/ehp.1510209.
109. Agency for Toxic Substances and Disease Registry. Toxicological Profile for Mercury. Atlanta, US: Public Health Services, 1999.
110. Clemens S, Monperrus M, Donard OF, Amouroux D, Guerin T. Mercury speciation analysis in seafood by species-specific isotope dilution: method validation and occurrence data. Analytical and bioanalytical chemistry 2011;401(9):2699-711. doi: 10.1007/s00216-011-5040-1.
111. Fabelova L, Vandentorren S, Vuillermoz C, Garnier R, Lioret S, Botton J. Hair concentration of trace elements and growth in homeless children aged <6years: Results from the ENFAMS study. Environ Int 2017. doi: 10.1016/j.envint.2017.10.012.
112. Marin S, Ramos AJ, Cano-Sancho G, Sanchis V. Mycotoxins: occurrence, toxicology, and exposure assessment. Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association 2013;60:218-37. doi: 10.1016/j.fct.2013.07.047.
113. IARC. IARC Monogrpahs on the evaluation of carcinogenic risks to humans: Some Traditional Herbal Medicines, Some Mycotoxins, Naphthalene and Styrene. Lyon, France, 2002.
114. Shuaib FM, Ehiri J, Abdullahi A, Williams JH, Jolly PE. Reproductive health effects of aflatoxins: a review of the literature. Reprod Toxicol 2010;29(3):262-70. doi: 10.1016/j.reprotox.2009.12.005.

115. Turner PC, Collinson AC, Cheung YB, et al. Aflatoxin exposure in utero causes growth faltering in Gambian infants. International journal of epidemiology 2007;36(5):1119-25. doi: 10.1093/ije/dym122.
116. Gong Y, Hounsa A, Egal S, et al. Postweaning exposure to aflatoxin results in impaired child growth: a longitudinal study in Benin, West Africa. Environ Health Perspect 2004;112(13):1334-8.
117. Asci A, Durmaz E, Erkekoglu P, Pasli D, Bircan I, Kocer-Gumusel B. Urinary zearalenone levels in girls with premature thelarche and idiopathic central precocious puberty. Minerva Pediatr 2014;66(6):571-8.
118. Bandera EV, Chandran U, Buckley B, et al. Urinary mycoestrogens, body size and breast development in New Jersey girls. The Science of the total environment 2011;409(24):5221-7. doi: 10.1016/j.scitotenv.2011.09.029.
119. Pestka JJ. Deoxynivalenol: mechanisms of action, human exposure, and toxicological relevance. Arch Toxicol 2010;84(9):663-79. doi: 10.1007/s00204-010-0579-8.
120. Smith LE, Stoltzfus RJ, Prendergast A. Food chain mycotoxin exposure, gut health, and impaired growth: a conceptual framework. Adv Nutr 2012;3(4):526-31. doi: 10.3945/an.112.002188.
121. Wu F, Groopman JD, Pestka JJ. Public health impacts of foodborne mycotoxins. Annu Rev Food Sci Technol 2014;5:351-72. doi: 10.1146/annurev-food-030713-092431.
122. IARC. IARC Monographs on the evaluation of carcinogenic risks to humans: Acrylamide. Lyon, France, 1994.
123. Duarte-Salles T, von Stedingk H, Granum B, et al. Dietary Acrylamide Intake during Pregnancy and Fetal Growth - Results from the Norwegian Mother and Child Cohort study (MoBa). Environ Health Perspect 2013;121:374-9. doi: 10.1289/ehp.1205396.
124. Pedersen M, von Stedingk H, Botsivali M, et al. Birth weight, head circumference, and prenatal exposure to acrylamide from maternal diet: the European prospective mother-child study (NewGeneris). Environ Health Perspect 2012;120(12):1739-45. doi: 10.1289/ehp.1205327.
125. Kadawathagedara M, Botton J, de Lauzon-Guillain B, et al. Dietary acrylamide intake during pregnancy and postnatal growth and obesity: Results from the Norwegian Mother and Child Cohort Study (MoBa). Environ Int 2018;113:325-34. doi: 10.1016/j.envint.2018.01.004.
126. Desai M, Jellyman JK, Ross MG. Epigenomics, gestational programming and risk of metabolic syndrome. International journal of obesity 2015;39(4):633-41. doi: 10.1038/ijo.2015.13.
127. Breton CV, Marsit CJ, Faustman E, et al. Small-Magnitude Effect Sizes in Epigenetic End Points are Important in Children's Environmental Health Studies: The Children's Environmental Health and Disease Prevention Research Center's Epigenetics Working Group. Environ Health Perspect 2017;125(4):511-26. doi: 10.1289/EHP595.
128. Bergman A, Becher G, Blumberg B, et al. Manufacturing doubt about endocrine disrupter science--A rebuttal of industry-sponsored critical comments on the UNEP/WHO report "State of the Science of Endocrine Disrupting Chemicals 2012". Regulatory toxicology and pharmacology : RTP 2015;73(3):1007-17. doi: 10.1016/j.yrtph.2015.07.026.
129. Newbold RR, Padilla-Banks E, Snyder RJ, Phillips TM, Jefferson WN. Developmental exposure to endocrine disruptors and the obesity epidemic. Reprod Toxicol 2007;23(3):290-6. doi: 10.1016/j.reprotox.2006.12.010.
130. Kabir ER, Rahman MS, Rahman I. A review on endocrine disruptors and their possible impacts on human health. Environ Toxicol Pharmacol 2015;40(1):241-58. doi: 10.1016/j.etap.2015.06.009.
131. Maqbool F, Mostafalou S, Bahadar H, Abdollahi M. Review of endocrine disorders associated with environmental toxicants and possible involved mechanisms. Life Sci 2016;145:265-73. doi: 10.1016/j.lfs.2015.10.022.
132. Heindel JJ, Newbold R, Schug TT. Endocrine disruptors and obesity. Nat Rev Endocrinol 2015;11(11):653-61. doi: 10.1038/nrendo.2015.163.

133. Heindel JJ, Blumberg B, Cave M, et al. Metabolism disrupting chemicals and metabolic disorders. Reprod Toxicol 2017;68:3-33. doi: 10.1016/j.reprotox.2016.10.001.
134. De Long NE, Holloway AC. Early-life chemical exposures and risk of metabolic syndrome. Diabetes Metab Syndr Obes 2017;10:101-9. doi: 10.2147/DMSO.S95296.
135. Diamanti-Kandarakis E, Bourguignon JP, Giudice LC, et al. Endocrine-disrupting chemicals: an Endocrine Society scientific statement. Endocr Rev 2009;30(4):293-342. doi: 10.1210/er.2009-0002.
136. Rodriguez-Rodriguez P, Ramiro-Cortijo D, Reyes-Hernandez CG, Lopez de Pablo AL, Gonzalez MC, Arribas SM. Implication of Oxidative Stress in Fetal Programming of Cardiovascular Disease. Front Physiol 2018;9:602. doi: 10.3389/fphys.2018.00602.
137. Carles S, Charles MA, Forhan A, et al. A Novel Method to Describe Early Offspring Body Mass Index (BMI) Trajectories and to Study Its Determinants. PloS one 2016;11(6):e0157766. doi: 10.1371/journal.pone.0157766.
138. Robinson O, Basagana X, Agier L, et al. The Pregnancy Exposome: Multiple Environmental Exposures in the INMA-Sabadell Birth Cohort. Environmental science & technology 2015;49(17):10632-41. doi: 10.1021/acs.est.5b01782.

***Table 2**: Summary of the literature on prenatal exposure to environmental contaminant's and child growth*

Prenatal exposure	Prenatal growth	Postnatal growth
Persistent Organic Pollutants (POPs)		
PCBs	No association: • 1 review (El Majidi et al., 2012) Negative association: • 1 MA of 14 cohorts studies N: 7,762 ; (Govarts et al., 2012)	No association: • 1 pooled analysis of 7 cohorts studies N: 2,487 ; (Iszatt et al., 2015)**
Dioxins and furans	Negative association: • 1 MA of 2 cohorts studies N: 9,455 ; (Pan et al., 2015)	Positive association: • 1 pooled analysis of 3 cohorts studies N: 367 ; (Iszatt et al., 2016)* and **
DDT/DDE	No association: • 3 cohort studies N: 420 ; (Farhang et al., 2005) N: 168 ; (Karmaus and Zhu, 2004) N: 912 ; (Rogan et al., 1986b) • 1 case-control study N: 157 ; (Dewailly et al., 1993) • 3 cross sectional studies N: 180 ; (Bjerregaard and Hansen, 2000) N: 197 ; (Gladen et al., 2003) N: 72 ; (Ribas-Fito et al., 2002) • 1 MA of 12 birth cohorts N: 7,530 ; (Govarts et al., 2012) Negative association: • 3 cohort studies N: 2,380 ; (Longnecker et al., 2001) N:858 ; (Rogan et al., 1986a) N: 143 ; (Weisskopf et al., 2005)	Positive association: • 1 pooled analysis of 7 cohorts studies N: 2,487 ; (Iszatt et al., 2015)*

	• 1 case-control study N:54 ; (Siddiqui et al., 2003)	
HCB	<u>No association:</u> • 3 cohort studies N: 385 ; (Fenster et al., 2006) N: 72 ; (Ribas-Fito et al., 2002) N: 722 ; (Sagiv et al., 2007) <u>Negative association:</u> • 3 cohort studies N: 81 ; (Guo et al., 2014) N: 494 ; (Lopez-Espinosa et al., 2011) N: 1,117 ; (Vafeiadi et al., 2014)	<u>No association:</u> • 1 review (Tang-Peronard et al., 2011) <u>Positive association:</u> • 1 cohort study N: 1,285 ; (Valvi et al., 2014)*
PBDEs	<u>No association:</u> • 1 review (Zheng et al., 2016)	<u>Positive association:</u> • 1 review (Vrijheid et al., 2016) with girls <u>Negative association:</u> • 1 review (Vrijheid et al., 2016) with boys
PFAS	<u>Negative association:</u> • 2 reviews (Bach et al., 2015) (Johnson et al., 2014)	<u>Positive association:</u> • 1 cohort study N: 447 ; (Maisonet et al., 2012)* <u>Negative association:</u> • 1 cohort study N: 1,400 ; (Andersen et al., 2010)* from 5mo to 12mo <u>No association:</u> • 1 cohort study N: 1,400 ; (Andersen et al., 2013)* at 7 years
Non POPs		
Phthalates	<u>No association:</u> • 2 reviews (Marie et al., 2015) (Vrijheid et al., 2016)	<u>No association:</u> • 1 review (Braun, 2017) • 1 cohort study N: 470 ; (Agay-Shay et al., 2015)* <u>Positive association</u> • 1 cohort study N: 520 ; (Botton et al., 2016)*
BPA	<u>No association:</u>	<u>No association:</u>

	• 2 reviews (Rochester, 2013) (Vrijheid et al., 2016) <u>Negative association:</u> • 1 cohort study N: 4,680 ; (Snijder et al., 2013)	• 1 cohort study N: 520 ; (Philippat et al., 2014)* <u>Positive association:</u> • 4 cross-sectional studies N: 2,200 ; (Bhandari et al., 2013)** N: 10, 990 ; (Eng et al., 2013)** N: 9,270 ; (Trasande et al., 2012)** N: 259 ; (Wang et al., 2012)** • 3 cohort studies N: 297 ; (Braun et al., 2014)* N: 402 ; (Valvi et al., 2013)* N: 500 ; (Vafeiadi et al., 2016)* in boys <u>Negative association:</u> • 1 cohort study N: 500 ; (Vafeiadi et al., 2016)* in girls
Other environmental phenols	<u>No association:</u> • 1 review (Slama and Cordier, 2013)	<u>Negative association:</u> • 1 cohort study N: 520 ; (Philippat et al., 2014)*, Triclosan
Toxic heavy metals		
Cadmium	<u>No association:</u> • 1 review (Slama and Cordier, 2013)	<u>No association:</u> • 1 review (Vrijheid et al., 2016) • 1 cross sectional study N: 324 ; (Fabelova et al., 2017)**
Lead	<u>No association:</u> • 1 review (Slama and Cordier, 2013)	<u>No association:</u> • 1 review (Vrijheid et al., 2016) • 1 cross sectional study N: 324 ; (Fabelova et al., 2017)**
Arsenic	<u>No association:</u> • 1 review (Slama and Cordier, 2013)	<u>No association:</u> • 1 review (Vrijheid et al., 2016) • 1 cross sectional study N: 324 ; (Fabelova et al., 2017)**
Mercury	<u>No association:</u> • 1 review (Slama and Cordier, 2013)	<u>No association:</u> • 1 review (Vrijheid et al., 2016)

			• 1 cross sectional study N: 324 ; (Fabelova et al., 2017)**
Other chemicals			
Mycotoxins			
	Aflatoxin	No association: • 1 review (Shuaib et al., 2010)	Negative association: • 2 cohort studies N: 138 (Turner et al., 2007)* N: 200 (Gong et al., 2004)**
	Zearalenone	No epidemiological studies	No association: • 1 case control study N: 78 ; (Asci et al., 2014)** • 1 cross sectional study N: 163 ; (Bandera et al., 2011)**
Acrylamide		Negative association: • 2 cohort studies N: 1,471 ; (Kadawathagedara et al., 2016) N: 50,651 ; (Duarte-Salles et al., 2013) • 1 consortium of cohort studies N: 1,001 ; (Pedersen et al., 2012)	Positive association: • 1 cohort study N: 51,952 ; (Kadawathagedara et al., 2018)*

MA: meta-analysis
Studies are only recent research articles not included in summarising articles
For postnatal growth association
*prenatal exposure
**postnatal exposure

Agay-Shay, K., et al., 2015. Exposure to Endocrine-Disrupting Chemicals during Pregnancy and Weight at 7 Years of Age: A Multi-pollutant Approach. Environ Health Perspect. 123**,** 1030-7.

Andersen, C. S., et al., 2010. Prenatal exposures to perfluorinated chemicals and anthropometric measures in infancy. Am J Epidemiol. 172**,** 1230-7.

Andersen, C. S., et al., 2013. Prenatal exposures to perfluorinated chemicals and anthropometry at 7 years of age. Am J Epidemiol. 178**,** 921-7.

Asci, A., et al., 2014. Urinary zearalenone levels in girls with premature thelarche and idiopathic central precocious puberty. Minerva Pediatr. 66**,** 571-8.

Bach, C. C., et al., 2015. Perfluoroalkyl and polyfluoroalkyl substances and human fetal growth: a systematic review. Crit Rev Toxicol. 45**,** 53-67.

Bandera, E. V., et al., 2011. Urinary mycoestrogens, body size and breast development in New Jersey girls. Sci Total Environ. 409, 5221-7.
Bhandari, R., et al., 2013. Urinary bisphenol A and obesity in U.S. children. Am J Epidemiol. 177, 1263-70.
Bjerregaard, P., Hansen, J. C., 2000. Organochlorines and heavy metals in pregnant women from the Disko Bay area in Greenland. Sci Total Environ. 245, 195-202.
Botton, J., et al., 2016. Phthalate pregnancy exposure and male offspring growth from the intra-uterine period to five years of age. Environ Res. 151, 601-609.
Braun, J. M., 2017. Early-life exposure to EDCs: role in childhood obesity and neurodevelopment. Nat Rev Endocrinol. 13, 161-173.
Braun, J. M., et al., 2014. Early-life bisphenol a exposure and child body mass index: a prospective cohort study. Environ Health Perspect. 122, 1239-45.
Dewailly, E., et al., 1993. Inuit exposure to organochlorines through the aquatic food chain in arctic quebec. Environ Health Perspect. 101, 618-20.
Duarte-Salles, T., et al., 2013. Dietary Acrylamide Intake during Pregnancy and Fetal Growth - Results from the Norwegian Mother and Child Cohort study (MoBa). Environ Health Perspect. . 121, 374-9.
El Majidi, N., et al., 2012. Relationship between prenatal exposure to polychlorinated biphenyls and birth weight: a systematic analysis of published epidemiological studies through a standardization of biomonitoring data. Regul Toxicol Pharmacol. 64, 161-76.
Eng, D. S., et al., 2013. Bisphenol A and chronic disease risk factors in US children. Pediatrics. 132, e637-45.
Fabelova, L., et al., 2017. Hair concentration of trace elements and growth in homeless children aged <6years: Results from the ENFAMS study. Environ Int.
Farhang, L., et al., 2005. Association of DDT and DDE with birth weight and length of gestation in the Child Health and Development Studies, 1959-1967. Am J Epidemiol. 162, 717-25.
Fenster, L., et al., 2006. Association of in utero organochlorine pesticide exposure and fetal growth and length of gestation in an agricultural population. Environ Health Perspect. 114, 597-602.
Gladen, B. C., et al., 2003. Persistent organochlorine compounds and birth weight. Ann Epidemiol. 13, 151-7.
Gong, Y., et al., 2004. Postweaning exposure to aflatoxin results in impaired child growth: a longitudinal study in Benin, West Africa. Environ Health Perspect. 112, 1334-8.
Govarts, E., et al., 2012. Birth weight and prenatal exposure to polychlorinated biphenyls (PCBs) and dichlorodiphenyldichloroethylene (DDE): a meta-analysis within 12 European Birth Cohorts. Environ Health Perspect. 120, 162-70.
Guo, H., et al., 2014. Prenatal exposure to organochlorine pesticides and infant birth weight in China. Chemosphere. 110, 1-7.
Iszatt, N., et al., 2016. Perinatal exposure to dioxins and dioxin-like compounds and infant growth and body mass index at seven years: A pooled analysis of three European birth cohorts. Environ Int. 94, 399-407.
Iszatt, N., et al., 2015. Prenatal and Postnatal Exposure to Persistent Organic Pollutants and Infant Growth: A Pooled Analysis of Seven European Birth Cohorts. Environ Health Perspect. 123, 730-6.
Johnson, P. I., et al., 2014. The Navigation Guide - evidence-based medicine meets environmental health: systematic review of human evidence for PFOA effects on fetal growth. Environ Health Perspect. 122, 1028-39.
Kadawathagedara, M., et al., 2018. Dietary acrylamide intake during pregnancy and postnatal growth and obesity: Results from the Norwegian Mother and Child Cohort Study (MoBa). Environ Int. 113, 325-334.
Kadawathagedara, M., et al., 2016. Dietary acrylamide intake during pregnancy and anthropometry at birth in the French EDEN mother-child cohort study. Environ Res. 149, 189-96.

Karmaus, W., Zhu, X., 2004. Maternal concentration of polychlorinated biphenyls and dichlorodiphenyl dichlorethylene and birth weight in Michigan fish eaters: a cohort study. Environ Health. 3**,** 1.

Longnecker, M. P., et al., 2001. Association between maternal serum concentration of the DDT metabolite DDE and preterm and small-for-gestational-age babies at birth. Lancet. 358**,** 110-4.

Lopez-Espinosa, M. J., et al., 2011. Prenatal exposure to organochlorine compounds and birth size. Pediatrics. 128**,** e127-34.

Maisonet, M., et al., 2012. Maternal concentrations of polyfluoroalkyl compounds during pregnancy and fetal and postnatal growth in British girls. Environ Health Perspect. 120**,** 1432-7.

Marie, C., et al., 2015. Obstetrical outcomes and biomarkers to assess exposure to phthalates: A review. Environ Int. 83**,** 116-36.

Pan, X., et al., 2015. Association between Environmental Dioxin-Related Toxicants Exposure and Adverse Pregnancy Outcome: Systematic Review and Meta-Analysis. Int J Fertil Steril. 8**,** 351-66.

Pedersen, M., et al., 2012. Birth weight, head circumference, and prenatal exposure to acrylamide from maternal diet: the European prospective mother-child study (NewGeneris). Environ Health Perspect. . 120**,** 1739-1745.

Philippat, C., et al., 2014. Prenatal exposure to phenols and growth in boys. Epidemiology. 25**,** 625-35.

Ribas-Fito, N., et al., 2002. Association of hexachlorobenzene and other organochlorine compounds with anthropometric measures at birth. Pediatr Res. 52**,** 163-7.

Rochester, J. R., 2013. Bisphenol A and human health: a review of the literature. Reprod Toxicol. 42**,** 132-55.

Rogan, W. J., et al., 1986a. Polychlorinated biphenyls (PCBs) and dichlorodiphenyl dichloroethene (DDE) in human milk: effects of maternal factors and previous lactation. Am J Public Health. 76**,** 172-7.

Rogan, W. J., et al., 1986b. Neonatal effects of transplacental exposure to PCBs and DDE. J Pediatr. 109**,** 335-41.

Sagiv, S. K., et al., 2007. Organochlorine exposures during pregnancy and infant size at birth. Epidemiology. 18**,** 120-9.

Shuaib, F. M., et al., 2010. Reproductive health effects of aflatoxins: a review of the literature. Reprod Toxicol. 29**,** 262-70.

Siddiqui, M. K., et al., 2003. Persistent chlorinated pesticides and intra-uterine foetal growth retardation: a possible association. Int Arch Occup Environ Health. 76**,** 75-80.

Slama, R., Cordier, S., 2013. [Impact of chemical and physical environmental factors on the course and outcome of pregnancy]. J Gynecol Obstet Biol Reprod (Paris). 42**,** 413-44.

Snijder, C. A., et al., 2013. Fetal growth and prenatal exposure to bisphenol A: the generation R study. Environ Health Perspect. 121**,** 393-8.

Tang-Peronard, J. L., et al., 2011. Endocrine-disrupting chemicals and obesity development in humans: a review. Obes Rev. 12**,** 622-36.

Trasande, L., et al., 2012. Association between urinary bisphenol A concentration and obesity prevalence in children and adolescents. Jama. 308**,** 1113-21.

Turner, P. C., et al., 2007. Aflatoxin exposure in utero causes growth faltering in Gambian infants. Int J Epidemiol. 36**,** 1119-25.

Vafeiadi, M., et al., 2016. Association of early life exposure to bisphenol A with obesity and cardiometabolic traits in childhood. Environ Res. 146**,** 379-87.

Vafeiadi, M., et al., 2014. Persistent organic pollutants exposure during pregnancy, maternal gestational weight gain, and birth outcomes in the mother-child cohort in Crete, Greece (RHEA study). Environ Int. 64**,** 116-23.

Valvi, D., et al., 2013. Prenatal bisphenol a urine concentrations and early rapid growth and overweight risk in the offspring. Epidemiology. 24**,** 791-9.

Valvi, D., et al., 2014. Prenatal exposure to persistent organic pollutants and rapid weight gain and overweight in infancy. Obesity (Silver Spring). 22**,** 488-96.

Vrijheid, M., et al., 2016. Environmental pollutants and child health-A review of recent concerns. Int J Hyg Environ Health. 219**,** 331-42.

Wang, H. X., et al., 2012. Association between bisphenol A exposure and body mass index in Chinese school children: a cross-sectional study. Environ Health. 11**,** 79.

Weisskopf, M. G., et al., 2005. Maternal exposure to Great Lakes sport-caught fish and dichlorodiphenyl dichloroethylene, but not polychlorinated biphenyls, is associated with reduced birth weight. Environ Res. 97**,** 149-62.

Zheng, T., et al., 2016. Effects of Environmental Exposures on Fetal and Childhood Growth Trajectories. Ann Glob Health. 82**,** 41-99.