Science of the Total Environment 609 (2017) 396–409

Contents lists available at ScienceDirect

Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv

Children's environmental health based on birth cohort studies of Asia

Meng-Shan Tsai [a], Mei-Huei Chen [b,c], Ching-Chun Lin [a], Sharon Ng [d], Chia-Jung Hsieh [e], Chen-yu Liu [f,h], Wu-Shiun Hsieh [c,g], Pau-Chung Chen [a,h,i,*]

[a] Institute of Occupational Medicine and Industrial Hygiene, National Taiwan University College of Public Health, Taipei, Taiwan
[b] Institute of Population Health Sciences, National Health Research Institutes, Miaoli, Taiwan
[c] Department of Pediatrics, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan
[d] Department of Obstetrics and Gynaecology, Yong Loo Lin School of Medicine, National University of Singapore, National University Health System, Singapore
[e] Department of Public Health, Tzu Chi University, Hualian County, Taiwan
[f] Institute of Environmental Health, College of Public Health, National Taiwan University, Taipei, Taiwan
[g] Department of Pediatrics, Cathay General Hospital, Taipei, Taiwan
[h] Department of Public Health, National Taiwan University College of Public Health, Taipei, Taiwan
[i] Department of Environmental and Occupational Medicine, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan

HIGHLIGHTS

- Environmental pollutants have adverse effects on Asia children.
- Mercury and PCB appear more evidence on children's neurodevelopment in Asia area.
- ETS, phthalate, and PFAS need more evidence related to children's health outcomes in Asia area.

ARTICLE INFO

Article history:
Received 23 March 2017
Received in revised form 14 June 2017
Accepted 10 July 2017
Available online 26 July 2017

Keywords:
Mercury
Environmental tobacco smoke
Polychlorinated biphenyls
Perfluoroalkyl substances
Phthalates
Birth cohort
Asia

ABSTRACT

Numerous studies have explored the associations between environmental pollutants and pediatric health. Recent studies have investigated the issue in Asia, but no systematic review has been published to date. This study aims to elucidate the issue by summarizing relevant epidemiologic evidence for cohorts in Asia, using information from the Birth Cohort Consortium of Asia (BiCCA).

Environmental pollutants include mercury, environmental tobacco smoke (ETS), polychlorinated biphenyls (PCB), perfluoroalkyl substances (PFAS) and phthalates. This study sought to classify the effects of such compounds on fetal growth and pregnancy outcomes, neurodevelopment and behavioral problems, allergic disease and immune function and the endocrine system and puberty. These evidences showed ETS has been associated with infant birth weight, children's neurodevelopment and allergy disease; mercury and PCB have been shown to affect children's neurodevelopment; phthalate has effects on endocrine function; PFAS alters children's neurodevelopment, the endocrine system, and the allergic response. However, more consistent and coordinated research is necessary to understand the whole picture of single environmental and/or co-exposure and children's health. Therefore, harmonization and international collaboration are also needed in Asia.

1. Introduction

In order to assess the consequences of prenatal exposure to environmental pollutants and identify the preventable risk factors, several large-scale birth cohort studies have been conducted worldwide (http://www.birthcohorts.net/). Birth cohort studies are those which begin at or before the birth of their subjects, and continue to study the same individuals at later ages, on more than one occasion. Birth cohort studies are a type of observational study in which there is no randomization to exposure classes or attempt to manipulate the exposure. The fetal programming hypothesis illustrated that external maternal malnourishment during pregnancy leads to lifelong, continuing adaptation of the fetus, which in turn results in low birth weight, increased cardiovascular risk, and non-insulin dependent diabetes in adult life (Barker et al., 1989). Developmental Origins of Health and Disease

* Corresponding author at: Institute of Occupational Medicine and Industrial Hygiene, National Taiwan University College of Public Health, 17 Xuzhou Road, Taipei 10055, Taiwan.
E-mail address: pchen@ntu.edu.tw (P.-C. Chen).

http://dx.doi.org/10.1016/j.scitotenv.2017.07.081
0048-9697/

(DOHaD) hypotheses posit that prenatal threats including environmental exposures are the origin of all disease and may impact human development (Heindel et al., 2015).

In recent years, air pollution (Lim et al., 2012), arsenic contamination of groundwater in Bangladesh (Mukherjee et al., 2006), melamine events leading to the concern of phthalates exposure may occur through food ingestion, air inhalation, and direct dermal contact with various types of products (Gossner et al., 2009; Wang et al., 2009; Chen et al., 2008), and the Fukushima Daiichi Nuclear Disaster (Yasumura et al., 2012) have aroused public attention in Asia. Birth Cohort Consortium of Asia (BiCCA) was established in 2011 to address these issues (http://www.bicca.org/). The BiCCA includes 23 birth cohorts, totaling approximately 70,000 study subjects, which conducted studies in 10 Asian countries. Over the last decade, BiCCA has already published a series of articles about the association between environmental pollutants and children's environmental health. In previous collaboration and investigation (Kishi et al., 2016), most participating cohorts on BiCCA have measured mercury, polychlorinated biphenyls (PCB), perfluoroalkyl substances (PFAS) and phthalates concentration on participant population and half of the cohorts collected information about environmental tobacco smoke (ETS) including second hand smoke; thence, this review focuses on these five pollutants.

ETS pollutant is common issue in worldwide but the issue is often overlooked. ETS can cause diseases, disability, and even death. Globally, 40% of children have been exposed to ETS; 28% of children died from ETS in 2004 (Oberg et al., 2011). Exposed to mercury has effects on the health of fetuses and children (Ginsberg et al., 2004). Previous studies have reported levels of individual PCB, total PCB, hydroxylated PCB metabolites (OH-PCB), and total OH-PCB (Marek et al., 2013; Park et al., 2009). The incidents in Yusho, Seveso, and Yucheng increased awareness about related health effects in children (Yoshimura et al., 2001). Phthalates and PFAS are endocrine disrupting chemicals (EDCs), which may cause adverse health effects (Agay-Shay et al., 2015). Phthalates may affect the human endocrine system triggering developmental problems caused by endocrine toxicity (Katsikantami et al., 2016). PFAS with longer half-lives bind to proteins in blood serum and accumulate and circulate in the organs of human body (Jensen and Leffers, 2008). On the other hand, most Asia countries experienced rapidly industrializing development and many western companies' manufacturing factories was built in Asia resulting in unconscious industrial disposal or emerging environmental pollutants. Gene sensitivity (Jorde and Wooding, 2004), life styles, and living environment (Olesen, 2004), and unsolid regulation of environmental chemicals (Sharma et al., 2014) are different from western countries. Moreover, several studies have examined the effects of these compounds on human health in Asia; therefore, this review aims to provide a summary of the relevant literature. We included research published by groups that were not part of the BiCCA to present a comprehensive investigation of the association between exposure to environmental pollutants and related effects on health of children.

2. Methods

We used the PubMed search engine (National Library of Medicine) to search and identify relevant articles about epidemiological studies of health outcomes and environmental exposure in Asia. The keyword used included different combinations of related to pregnancy women, children health outcomes, and environmental pollutants as the following. Various keywords culled from the literature review were used to investigate population, exposure, and outcomes.

Keywords for population were: pregnancy; pregnant; birth; toddler; child; children; childhood. Keywords for Asia area were: Abkhazia; Afghanistan; Armenia; Azerbaijan; Bahrain; Bangladesh; Bhutan; Brunei; Cambodia; China; East Timor; India; Indonesia; Iran; Iraq; Israel; Japan; Jordan; Kazakhsta; Kuwait; Kyrgyzstan; Laos; Lebanon; Malaysia; Maldives; Mongolia; Myanmar; Nagorno-Karabakh; Nepal; Northern Cyprus; North Korea; Oman; Pakistan; Palestine; Philippines; Qatar; Saudi Arabia; Singapore; South Korea; South Ossetia; Sri Lanka; Syria; Taiwan; Tajikistan; Thailand; Turkey; Turkmenistan; United Arab Emirates; Uzbekistan; Vietnam; Yemen.

Keywords for exposure were: tobacco smoke; biomass smoke; second hand smoke; heavy metal; mercury endocrine disruptor; persistent organic pollutant; polychlorinated biphenyl (PCB); organochlorine compound (OCs); hexachlorobenzene (HCB); perfluoroalkyl substance (PFAS); perfluorinated compound; perfluoroalkyl acid; perfluorooctane sulfonate (PFOS); perfluorooctanoate (PFOA); and phthalate.

Keywords for outcomes were: birth outcome; birth weight; fetal growth; birth size; preterm birth; gestational duration; gestational length; birth defect; congenital malformation; neurodevelopment; cognition; autism; attention deficit hyperactivity disorder; allergy; asthma; wheeze; lung function; bronchitis; pneumonia; respiratory tract infection; immune system; postnatal growth; obesity; body mass index; waist circumference; dyslipidemia; lipids; cholesterol; triglycerides; diabetes; insulin; glucose; hypertension; blood pressure; endocrine function; puberty; and pre-puberty.

The literature search covered a period extending through January 31, 2017 with no other restrictions on the date of publication. We included articles that investigated prenatal/maternal, in utero exposures, or postnatal childhood exposure. All articles were based on birth cohort studies and published in the English language.

Articles investigating co-exposure to other environment pollutants were included in the present study. Ultimately, exposure to five compounds was investigated. Children's health outcomes were classified to one of four categories: fetal growth and pregnancy outcome, neurodevelopment and behavioral problems, allergic disease and immune function and endocrine function and puberty. Fetal growth and pregnancy outcomes included birth weight, birth length, head circumference, and gestational age by questionnaire and physical examination. Information related to all outcomes was collected by questionnaire and physical examination.

3. Environmental tobacco smoke (ETS)

Table 1 shows that association between ETS exposure, fetal growth and pregnancy outcomes, neurodevelopment and behavioral problems, and allergic disease and immune function. Birth weight was the common measurement on all cohorts, and ISAAC questionnaire was used by three cohorts, but neurodevelopment and behavioral questionnaires varied from different birth cohorts.

3.1. Fetal growth and pregnancy outcomes

Five birth cohort studies explored the association between ETS and birth weight. Two studies investigated the association between ETS and birth weight including the genetic effects. The results of a study conducted on 1388 newly married mothers of liveborn singletons in Anqing, China showed that 2 maternal metabolic genes, cytochrome P-450 1A1 (CYP1A1) MspI and epoxide hydrolase 1 (EPHX1) Tyr113His were involved in the association of self-reported passive smoke exposure during pregnancy and infant birth weight (Wu et al., 2007). Another study explored 1784 native Japanese mother-child pairs from Hokkaido study. The results showed that maternal 5,10-MTHFR C677T polymorphism was independently associated with improvement in infant birth weight among nonsmokers. However, 5,10-MTHFR 1298AA might be associated with folate impairment and could be also associated with ETS exposure during pregnancy on reducing infant birth weight (Yila et al., 2012). Two studies on ETS also explored the effects of active smoking on birth weight and gestational condition. Miyake et al. (2013) reported that maternal smoke during pregnancy increased the risk of a child being born small for gestational age (SGA) and decreased birth weight (Miyake et al., 2013). Using data from a national birth cohort in Taiwan (N = 21,248), Ko et al. (2014) found that maternal smoking

Table 1
Association between environmental tobacco smoke (ETS) and children's health outcomes.

Birth cohort, nationality	Year	Mother-infant	Exposure	Main outcome	Results	Association	Reference
Fetal growth and pregnancy outcome							
Anqing, China	2007	1388	Questionnaire from the first, second, and third trimesters.	BW, polymorphisms in maternal metabolic genes	CYP1A1 MspI (C/C6235) and EPHX1 (Tyr/His113) genotypes modified the association between maternal passive smoking and decreased infant BW.	β = −156.3 g (CI −283.6 to −29); β = −93.8 g (CI −188.6 to −1.1)	Wu et al., 2007
Tamil Nadu, India	2009	11,728	Enrolment questionnaire of cooking fuel and parent smoking	Birth: GA, BW. 2 weeks after delivery: morbidity. 6 months: anthropometric measurements	Exposure to biomass fuel and ETS was associated with increased risk of LBW, respiratory illness, and 6-month infant mortality	49%, 34%, 21%	Tielsch et al., 2009
Hokkaido, Japan	2012	1784	Postpartum questionnaires of active and passive exposure during pregnancy	First trimester for serum folate assays, SNPs, BW	Offspring of smokers 5,10-methylenetetrahydrofolate reductase (MTHFR) associated with decrease BW.	β = −107.0 g (CI −180 to −33.9)	Yila et al., 2012
KOMCHS, Japan	2013	1565	Questionnaires in the first, second, and third trimesters	BW, SGA	Active maternal smoking throughout pregnancy, but not during the first trimester, is significantly associated with an increased risk of SGA.	OR = 2.87 (CI 1.11–6.56)	Miyake et al., 2013
TBCS, Taiwan	2014	21,248	Questionnaire 6 months after delivery for first, second, and third trimesters exposure	BW, SGA	Maternal smoking (>20 cigarettes/day) during second and third trimester increased incidences of LBW and SGA infants	LBW OR = 6.33 (CI 1.6–25); SGA OR = 3.87 (CI 1.01–214.82);	Ko et al., 2014
Hokkaido, Japan	2016	3263	Cotinine levels during the third trimester	BW, birth length, and head circumference, maternal genotypes	Infants' mothers smoking during pregnancy with AHR-GG, CYP1A1-AG/GG, and XRCC1-CT/TT polymorphisms had LBW.	β = −145 g (CI −241 to −50)	Kobayashi et al., 2016
Neurodevelopment and behavioral problems							
TBPS, Taiwan	2008	145	Cord blood cotinine, questionnaire after 3 days delivery	CDIIT at 2 years of age, gene polymorphisms	Infant with CYP1A1 Ile462Val and GSTT1 modify the effect of cord blood cotinine on neurodevelopment (development quotients) at 2 years of age.	Language β = −12.4 p = 0.006	Hsieh et al., 2008
TBPS, Taiwan	2010	191	Cord blood cotinine, questionnaire after 3 days delivery	CBCL at 2 years of age, gene polymorphisms	Infant with CYP1A1(MspI and Ile462Val) modifies the effect of maternal exposure to ETS on child behavior at 2 years of age.	β = 7.27 ± SE3.68; β = 6.53 ± SE3.08	Hsieh et al., 2010
TBPS, Taiwan	2011	87	Cord blood cotinine, questionnaire after 3 days delivery	NNE-C within three days after delivery	Weaker responses in neonatal primitive reflexes (grasp and tonic neck) in infants with the absent type GSTM1 were related to maternal ETS exposure during pregnancy.	β = −0.35 ± SE 0.14; β = −0.40 0 ± SE.18	Hsieh et al., 2011
MOCEH, Korea	2011	414	Questionnaire during pregnancy and at 6 months postpartum.	BSID-II at 6 months	The infants of non-smoking women exposed to ETS are at risk of neurodevelopmental (mental developmental index >85) delay.	OR = 2.36 (CI 1.21 to 4.59)	Lee et al., 2011
Chongqing, China	2012	122	Questionnaire after delivery for exposure, cord blood samples for PAH-DNA adducts.	WPPSI at age 5	Exposure of pregnant women to emissions of PAHs from the coal-burning plant, in combination with prenatal exposure to ETS, may have adversely affected cognitive function (full scale) of children at age 5.	β = −10.10 (CI −18.9 to −1.29)	Perera et al., 2012
Allergic disease and immune function							
TBPS, Taiwan	2008	261	Questionnaires at birth for pregnancy exposure, cord blood cotinine	ISAAC at 2 years of age	Smoke exposure during pregnancy (maternal blood cotinine >1.4563 ng/ml; cord blood cotinine) might increase the risk of atopic dermatitis in children.	OR = 5.33 (CI 1.33 to 21.41); OR = 5.71 (CI 1.40 to 23.32)	Wang et al., 2008
KOMCHS, Japan	2008	763	Questionnaires at 2 to 9 months post-delivery	ISAAC at16 to 24 months of age	Postnatal maternal smoking might be associated with an increased risk of wheeze in Japanese infants.	22.1%	Tanaka et al., 2008
KOMCHS, Japan	2012	1743 pregnant women	Questionnaire during pregnancy for exposure history	European Community Respiratory Health Survey: wheeze and asthma, ISAAC: eczema and rhinoconjunctivitis	Postnatal maternal smoking (pack-years of smoking ≥4.0), but not perinatal ETS might be associated with an increased risk of wheeze in Japanese infants.	OR = 1.93 (CI 1.30 to 2.83)	Tanaka et al., 2012
GEIBCS, Taiwan	2012	794	Questionnaire during pregnancy for exposure history	Cord blood IgE, genotyping	The influence of IL-13 genetic variants on cord blood IgE elevation was modified by male sex and prenatal ETS.	OR = 2.81 (CI 1.54 to 5.15)	CH Chen et al., 2012a
TBCS, Taiwan	2012	21,248	Questionnaire at the age of 6 months for exposure history	Structured questionnaire	Preterm birth, congenital cardiopulmonary disease, antibiotic use during pregnancy, maternal overweight, daily prenatal exposure to ETS, maternal smoking during pregnancy, and visible mould on walls at home are risk factors associated with infantile pneumonia.	OR = 2.43 (CI 1.16 to 4.72)	Chen et al., 2012c

Birth weight (BW), low birth weight (LBW), gestational age (GA), single nucleotide polymorphisms (SNPs), small-for-gestational-age (SGA), Neonatal Neurobehavioral Examination-Chinese Version (NNE-C), International Study of Asthma and Allergies in Childhood (ISAAC), Comprehensive Developmental Inventory for Infants and Toddlers (CDIIT), Bayley Scales of Infant Development—second edition (BSID-II), Wechsler Preschool and Primary Scale of Intelligence (WPPSI), Child Behavior Checklist (CBCL).

increased the risk for low birth weight, SGA, and preterm birth (Ko et al., 2014). A population-based cohort study recruited 11,728 live-born in Tamil Nadu, India. The author found that exposure to ETS during pregnancy was associated not only with low birth weight but also with respiratory illness and 6-month infant mortality (Tielsch et al., 2009). In addition, birth size related to birth weight were also considered in the study. Recently, Hokkaido study collected 3263 participants who were divided into 2 groups including 1998 non-smokers and 1265 smokers. They explored the effects of gene polymorphisms and smoking on birth size. The study revealed that prenatal maternal smoking and fetal AHR-GG, CYP1A1-AG/GG, and XRCC1-CT/TT genotypes were associated with lower birth weight (Kobayashi et al., 2016).

3.2. Neurodevelopment and behavioral problems

One birth cohort study investigated polycyclic aromatic hydrocarbons (PAH) and ETS exposure in 149 mother–child pairs with Shanghai version of Wechsler Preschool and Primary Scale of Intelligence (1985). The results showed that maternal exposure to PAH and ETS during pregnancy may have adverse effects on children's cognitive function as measured at the age of 5 years among children in Chongqing, China (Perera et al., 2012). The other study collected 414 mother-infant pairs from the Mothers' and Children's Environmental Health. Children were evaluated with Bayley Scales of Infant Development at 6 months of age. The results showed that ETS exposure during pregnancy was related to an increased risk of delayed mental development (Lee et al., 2011). Taiwan Birth Panel Study (TBPS) published a series of papers about genetic modification by ETS and associated effects on the neurodevelopment and behavior of children. The effect of cotinine cord blood on neurodevelopment (especially for language and fine motor development) was measured with the Comprehensive Developmental Inventory for Infants and Toddlers (CDIIT) (Wang et al., 1998). The findings showed effects on 2 metabolic genes (CYP1A1 and GSTT1) at age 2 years based on 145 children (Hsieh et al., 2008). CYP1A1from 191 children also modified the effect of prenatal maternal ETS exposure and behavior assessed by Child Behavior Checklist/1.5-5 (CBCL/1.5/5) at 2 year of age (Hsieh et al., 2010). On the other hand, 87 neonate's primitive reflexes at the age of 3 days revealed that prenatal maternal ETS exposure was also related to adverse effects on neurobehavioral development of infants without GSTM1 allele (Hsieh et al., 2011).

3.3. Allergic disease and immune function

Two cohort studies conducted in Japan found that postnatal maternal smoking increased the risk for wheezing: Osaka Maternal and Child Health Study (OMCHS) included 763 infants (Tanaka et al., 2008); the Kyushu Okinawa Maternal and Child Health Study (KOMCHS) included 1743 pregnant women (Tanaka et al., 2012). Before that, TBPS found that maternal smoke and exposure to ETS may increase the risk of atopic dermatitis in children in Taiwan based on 261 participants (Wang et al., 2008). Another study conducted in population from Taiwan (n = 21,248) found that daily prenatal exposure to ETS and maternal smoking during pregnancy was associated with infantile pneumonia (Chen et al., 2012b). The Gene and Environment Interaction Birth Cohort Study (GEIBCS) conducted in Taiwan the effects of gene and sex. A total of 794 neonates' information was collected with questionnaires and measurements of cord blood IgE (cIgE). The results showed that male sex and prenatal ETS modified the effect of IL-13 on cIgE levels.

4. Mercury

The association between mercury exposure, fetal growth and pregnancy outcomes, children growth, and neurodevelopment and behavioral problems shows in Table 2. However, only one evidence reported the effect on children growth and allergic disease and immune function. Birth weight was measured by all cohorts, but measurement of children's neurodevelopment and behavioral questionnaires were different.

4.1. Fetal growth and pregnancy outcomes

Although several studies have found associations between exposure to mercury and fetal and pregnancy outcomes, the results are conflicting. In Korea, Mothers and Children's Environmental Health (MOCEH) explored the effect of gene polymorphisms on exposure to mercury and birth weight in 417 mother–infant pairs. The results showed that maternal smoking during early and late pregnancy and cord blood mercury levels were associated with lower birth weight in mothers without the GSTM1/GSTT1 allele (Lee et al., 2010). However, three other studies found no association between mercury exposure and birth outcomes, or between mercury exposure and neonatal anthropometrics such as birth weight, length, and head circumference (Guo et al., 2013; Hu et al., 2015; Miyashita et al., 2015).

In addition, there was only a study investigated the association between mercury and children's growth. The MOCEH collected 797 children found that the weights attained by infants over the first 24 months of age were inversely associated with maternal smoking during early and late pregnancy and cord blood mercury levels (Kim et al., 2011a).

4.2. Neurodevelopment and behavioral problems

A recent study found no significant association between prenatal mercury concentration and neurodevelopment at 12 months. The study included 410 mother–infant pairs from rural northern China, who were evaluated using Gesell Developmental Schedules (GDS) (Hu et al., 2016). At age of 2 years, TBPS (n = 168) used the CDIIT to show that neurodevelopment (especially on cognition and social tests) was affected by cord blood mercury and modified by ApoE (Ng et al., 2013). CBCL testing showed that ApoE modifies the adverse effects of cord blood mercury on child behavior (including general internalization, emotional reactivity, and anxiety/depression) (Ng et al., 2015). Another study that evaluated 83 mother–infant pairs in Taiwan found no association between prenatal mercury and results on the Bayley Scales of Infant and Toddler Development (Bayley-III), which was administered to children at the age of 3 years (Hsi et al., 2014). However, the Tohoku Study of Child Development (TSCD) reported no association between child behavior and cord blood mercury levels, based on the results of CBCL testing in 306 children aged 2 to 3 years (Tatsuta et al., 2012). In the same cohort, maternal hair levels of MeHg (measured 2 days after delivery) were inversely correlated with neonatal neurobehavioral function (motor scores) as assessed by the Neonatal Behavioral Assessment Scale (NBAS) (Suzuki et al., 2010).

Our literature search revealed only one study that had explored effects on allergy and immune function. The Osaka Maternal and Child Health Study (OMCHS) reported no association between mercury levels in the hair of mothers or children (29–39 months postpartum) and the risk of wheeze or eczema in children aged 29–39 months (Miyake et al., 2011).

5. Polychlorinated biphenyls (PCB)

Table 3 presents the PCB exposure evidences of fetal growth and pregnancy outcomes, neurodevelopment and behavioral problems, and endocrine function and puberty. Different birth outcomes, and neurodevelopment and behavioral questionnaires were measured by different cohorts, but thyroid hormones of thyroid stimulating hormone (TSH), thyroxine (T4), and triiodothyronine (T3) were measured by three cohorts.

Table 2
Association between mercury and children's health outcomes.

Birth cohort, nationality	Year	Mother-infant	Exposure	Main outcome	Results	Association	Reference
Fetal growth and pregnancy outcome							
MOCEH, Korea	2010	417	Maternal blood during early pregnancy (12–20 gestational weeks) and late pregnancy (28–42 gestational weeks).	BW, GA, polymorphisms	The interactions of Hg without GSTM (cord blood) and GSTT1 (late pregnancy) polymorphisms play a role in reducing BW.	β = −107.3 (CI −199.7 to −14.8); β = −99 (CI −189.2 to −8.8)	Lee et al., 2010
Jiangsu, China	2013	213	Maternal and fetal hair within 3 days after delivery, placentas, cord blood	BW, body length, and head circumference	No significant correlations were found between Hg levels in maternal hair, fetal hair, placenta, or cord blood and neonatal anthropometrics.	No association	Guo et al., 2013
Hokkaido, Japan	2015	367	Total mercury in hair during pregnancy and at delivery	BW, SGA, birth length, chest circumference, and head circumference.	No overall association between mercury concentrations and BW, birth length, chest circumference, and head circumference. The risk of SGA by weight decreased with increasing mercury concentration (adjust for polyunsaturated fatty acids)	SGA by weight OR = 0.16 (CI 0.03 to 0.77)	Miyashita et al., 2015
LWBC, China	2015	81	Maternal and cord blood	BW	No significant associations were found between maternal or cord blood Hg levels and BW, length, and head circumference.	No association	Hu et al., 2015
Children growth							
MOCEH, Korea	2011	797	Maternal blood during early pregnancy (12–20 gestational weeks) and late pregnancy (28–42 gestational weeks).	Weight	Cord blood mercury negatively associated with infant's attained weight over the first 24 months of age.	β = −0.36 (CI −0.62 to −0.10)	Kim et al., 2011a
Neurodevelopment and behavioral problems							
TSCD, Japan	2010	498	Maternal hair 2 days after delivery,	NBAS at 3 days of age	Prenatal exposure to methylmercury adversely affects neonatal neurobehavioral function (motor).	β = −0.090 $p < 0.05$	Suzuki et al., 2010
TSCD, Japan	2012	306	Cord blood	CBCL at age of 2-to 3-year-old	No significant correlation was seen between any CBCL score and either Total Hg or lead.	No association	Tatsuta et al., 2012
TBPS, Taiwan	2013	168	Cord blood	CDIIT at age of 2	APOE modifies the adverse effects of cord blood Hg on neurodevelopment (whole test) at the age of 2 years.	β = −10.45 (CI −17.36 to −3.54)	Ng et al., 2013
Taipei, Taiwan	2014	83	Meconium after delivery and toenail, fingernail, and hair samples of children at three years of age	Bayley-III at age of 3	The prenatal mercury exposure did not show significant influence on neurological development.	No association	Hsi et al., 2014
TBPS, Taiwan	2015	166	Cord blood	CBCL at age of 2	APOE (ε4 carrier) modifies the adverse effects of cord blood Hg (≥12 μg/L) on child behavior (internalizing) at the age of 2 years.	β = 5.6 ± SE2.1 $p = 0.01$	Ng et al., 2015
LWBC, China	2016	410	Maternal blood prior to delivery, cord blood	GDS at the age of 1 year old.	No adverse effects between prenatal Hg exposure and infant neurodevelopment.	No association	Hu et al., 2016
Allergic disease and immune function							
Osaka, Japan	2011	582	Mother and child from 29 to 39 months postpartum	ISAAC phase-I	No evidence that hair mercury levels in either mothers or children are positively associated with the risk of wheeze or eczema in children aged 29–39 months in Japan, where fish intake is high.	No association	Miyake et al., 2011

Birth weight (BW), low birth weight (LBW), gestational age (GA), single nucleotide polymorphisms (SNPs), small-for-gestational-age (SGA), Neonatal Neurobehavioral Examination-Chinese Version (NNE-C), International Study of Asthma and Allergies in Childhood (ISAAC), Comprehensive Developmental Inventory for Infants and Toddlers (CDIIT), Bayley Scales of Infant Development—second edition (BSID-II), Wechsler Preschool and Primary Scale of Intelligence (WPPSI), Neonatal Behavioral Assessment Scale (NBAS), Gesell developmental schedules (GDS), Child Behavior Checklist (CBCL).

5.1. Fetal growth and pregnancy outcomes

Wu et al. (2011) and Xu et al. (2015) published two studies about the association between PCB and fetal growth in Guangdong e-waste recycling towns in China (Wu et al., 2011; Xu et al., 2015). Wu et al. (2011) found high levels of cord blood PCB congeners to be associated with reduced fetal physical development, especially neonatal birth weight. Xu et al. (2015) investigated gene expression and found that total cord blood PCB was inversely associated with increased KISS1 mRNA expression. However, Hisada et al. (2014) reported no association between maternal levels of OH-PCB/PCB isomers during the first trimester and neonatal birth size (based on 79 mother–infant pairs). (Hisada et al., 2014). In a study of 367 mother–infant pairs, Miyashita et al. (2015) found no association between maternal total PCB during the last trimester and birth size (Miyashita et al., 2015). Tsuji et al. (2013) found that maternal levels of PCB in the first trimester and cord blood PCB level were positively associated with placental growth factor levels as well as total estimated syncytiotrophoblast volume (Tsuji et al., 2013).

5.2. Neurodevelopment and behavioral problems

Two studies found no association between PCB and children's neurobehavioral problems. One hundred and thirty-five mother–infant pairs were assessed with the BSID-II found no association between maternal PCB during the last pregnancy and the mental or motor development at children aged 6 months (Nakajima et al., 2006). The Tohoku Study of Child Development (TSCD), which included 498 mother–infant pairs, also found no association between cord blood PCB and neurobehavioral function as measured by NBAS at the age of 3 days (Suzuki et al., 2010). However, a study of 306 children in the same cohort found that cord blood PCB levels could predict a child's internalizing behavior as measured with the CBCL at the age of 2–3 years (Tatsuta et al., 2012). The TSCD study of 387 mother–infant pairs found that cord blood levels of highly chlorinated PCB homologs could predict sequential and mental processing scores on the Kaufman Assessment Battery for Children (K-ABC) (Kaufman and Kaufman, 1983) in children aged 42 months,

Table 3
Association between polychlorinated biphenyl (PCB) and children's health outcomes.

Birth Cohort, Nationality	Year	Mother-infant	Exposure	Main outcome	Results	Association	Reference
Fetal growth and pregnancy outcome							
Guangdong, China	2011	167	Cord blood	Height, weight, BMI, GA, and Apgar score	Individual PCB congeners associated with reduced fetal physical development in e-waste recycling towns.	Height [CB 114 ($r = -0.19$), CB108 ($r = -0.28$)]; Weight [CB 138 ($r = -0.29$), CB153 ($r = -0.30$), CB180 ($r = -0.30$)]	Wu et al., 2011
JECS (Fukuoka), Japan	2013	22	Maternal in the first trimester and cord blood	Placenta PlGF and ST	Significant associations between PCB exposure and both increased PlGF and decreased total estimated ST volume were identified.	Maternal: $\beta = 2.86 \pm SE0.82$; Cord blood: $\beta = 3.74 \pm SE0.88$	Tsuji et al., 2013
Tokyo, Japan	2014	79	Maternal blood during the first trimester	Birth size	There were no significant associations between OH-PCBs/PCBs and body size of neonates.	No association	Hisada et al., 2014
Guangdong, China	2015	200	Cord blood	Neonatal outcomes, placental gene expression	Newborns in e-waste recycling towns have a lower birth weight that is inversely associated with blood level of Cd and PCBs, and may result from the increased KISS1 mRNA expression.	$\beta = -0.127$,$t = -2.08$, $p = 0.039$	Xu et al., 2015
Hokkaido, Japan	2015	367	Maternal blood during the last trimester	Birth size	The concentrations of PCBs had no association with birth size.	No association	Miyashita et al., 2015
Neurodevelopment and behavioral problems							
Hokkaido, Japan	2006	134	Maternal blood after the second trimester during their last pregnancy.	BSID-II at 6 months of age.	No significant association between the maternal blood PCB/dioxin level and mental and motor development, whereas significant negative associations with the levels of some isomers of dioxins and mental and motor development.	No association	Nakajima et al., 2006
TSCD, Japan	2010	498	Cord blood	NBAS at 3 days after birth	The neurobehavioral effect (motor) of prenatal exposure to PCBs remains not confirmed in this study.	No association	Suzuki et al., 2010
TSCD, Japan	2012	306	Cord blood	CBCL at age of 2–3	Internalizing behavior appears to be affected by prenatal exposure to PCBs at low levels.	$r = 0.158$, $p < 0.05$	Tatsuta et al., 2012
Nagasaki, Japan	2013	40	Cord blood	Upright and inverted biological motion and KIDS questionnaire at age of 4 months	Prenatal exposure to PCB congener influences expression language at 4-months-old.	PCB156: $r = -0.42$; PCB199: $r = -0.48$ $p < 0.05$	Doi et al., 2013
TSCD, Japan	2014	387	Cord blood	K-ABC at age of 42 months	The sequential and mental processing score of the K-ABC in the developmental stage may be impaired by prenatal exposures to highly chlorinated PCB homologs, especially in Japanese boys.	$\beta = -8.17$ (CI −15.24 to −1.11); $\beta = -6.79$ (CI −12.81 to −0.77);	Tatsuta et al., 2014
Endocrine function and puberty							
TMICS, Taiwan	2012	56	Placenta	T, E2, LH, FSH, TG, cholesterol, and insulin	In utero exposure to high levels of PCBs and PCDD/Fs may result in lower estradiol concentrations in 8 year-old children and impaired reproductive development (uterus length) in girls.	OR = 0.06 (CI 0.01 to 0.59)	Su et al., 2012
CHECK, Korea	2013	105 pregnant women	Pregnant women	fT3,T3, fT4, T4, and TSH in pregnant women	Several PCBs are negatively associated with T3 or T4 levels.	$\beta = -0.12$ (CI −0.20 to −0.04); $\beta = -0.06$ (CI −0.11 to −0.002);	Kim et al., 2013
Tokyo, Japan	2013	129 pregnant women	Pregnant women	fT4, TSH and TBG in pregnant women	Exposure/body burden of OH-PCBs and PCBs at environmental levels does not have a measurable effect on thyroid hormones.	No association	Hisada et al., 2013
Tokyo, Japan	2014	79	Maternal blood during the first trimester	TSH and fT4 in the neonatal whole blood	A significant positive association between the concentrations of OH-PCBs isomers and that of neonatal TSH.	$\beta = 0.235$, $p = 0.037$	Hisada et al., 2014
CHECK, Korea	2015	104	Cord blood	fT3,T3, fT4, T4, and TSH in cord blood	No significant association between prenatal PCBs exposure and thyroid hormone levels among newborn infant population.	No association	Kim et al., 2015
TMICS, Taiwan	2015	56	Placenta	T3, T4, fT4, TSH, TBG, IGF-1, and IGFBP-3	The high level of in utero exposure to PCBs and dioxins may affect serum concentrations of growth hormone and thyroxine-binding globulin in 8-year-old children.	OR = 65.84 (CI 1.16 to 29.39); OR = 7.65 (CI 1.34 to 43.61)	Su et al., 2015b

Body mass index (BMI), gestational age (GA), placental growth factor (PlGF), syncytiotrophoblast (ST), Bayley Scales of Infant Development—second edition(BSID-II), Behavioral Assessment Scale (NBAS), Child Behavior Checklist (CBCL), Kinder Infant Development Scale (KIDS), Kaufman Assessment Battery for Children (K-ABC), testosterone (T), estradiol (E2), luteinizing hormone (LH), follicle-stimulating hormone (FSH), triglyceride (TG), thyroxine binding globulin (TBG), thyroid stimulating hormone (TSH), free thyroxine (fT4), thyroxine (T4), triiodothyronine (T3), free triiodothyronine (fT3), insulin-like growth factor-1 (IGF-1), IGF-binding protein-3 (IGFBP-3).

especially for boys (Tatsuta et al., 2014). In a study of 40 infants, Doi et al. (2013) found that cord blood levels of PCB congeners influenced the duration of fixation on biological motion at the age of 4 months (Doi et al., 2013).

5.3. Endocrine function and puberty

Two studies have reported an association between PCB and thyroid hormone. As part of a Children's Health and Environmental Chemicals

in Korea (CHECK) study, Kim et al. (2013) measured maternal blood levels of PCB one day before delivery and found a negative association with T3 and T4 in 105 pregnant women (Kim et al., 2013). Hisada et al. (2014) reported that maternal first trimester blood levels of OH-PCBs and PCB were positively associated with levels of neonatal thyroid stimulating TSH in 79 mother–infant pairs in Japan (Hisada et al., 2014). However, two studies found no association between PCB and thyroid hormone. One examined the association between OH-PCBs/PCBs and thyroid hormone in 129 pregnant women at 10–12 gestational weeks (Hisada et al., 2013). The other found no association between levels of PCB in cord blood or maternal blood during delivery and thyroid hormone levels in cord blood after examining 104 newborns in Korea. (Kim et al., 2015). A report from the Taiwan Maternal and Infant Cohort Study (TMICS), based on the analysis of 56 children at 8 years of age, found that placental levels of PCB and dioxins may affect serum concentrations of growth hormone, thyroid hormone, thyroxine-binding globulin, and IGF-binding protein-3(Su et al., 2015b). The authors also found that higher placental levels of PCB and dioxin were associated with lower levels of estradiol in 8-year-old children and impaired reproductive development in girls (Su et al., 2012).

6. Phthalates

Table 4 reports the association of fetal growth and pregnancy outcomes, neurodevelopment and behavioral problems, endocrine function and puberty, and allergic disease and immune function from phthalates exposure. Two cohorts explored the effects on fetal growth, used BSID-II to measure the child development, and measured allergy disease by ISAAC questionnaire. Three cohorts measured E2 as outcomes to explore endocrine function.

6.1. Fetal growth and pregnancy outcome

To date, only two studies have focused on phthalate exposure and fetal growth. Kim et al. (2016) found that higher levels of DEHP metabolites in the urine of newborns were associated with lower scores on the Ponderal Index and increased levels of triglyceride at birth. Body mass increase was accelerated in newborn infants exposed to DEHP in 128 CHECK mother–infant pairs (Kim et al., 2016). Recently, Minatoya et al. (2017) reported that maternal blood levels of MEHP during the third trimester were positively associated with adiponectin levels in boys and negatively associated with leptin levels in girls (Minatoya et al., 2017).

6.2. Neurodevelopment and behavioral problems

Kim et al. (2011a, 2011b) found that levels of MEHHP, MEOHP, and MBP in maternal urine during the third trimester were inversely correlated with Mental and Psychomotor Developmental Indices (MDI and PDI, respectively) on the BSID-II at 6 months, especially for males from the MOCEH study of 460 mother–infant pairs in Korea (Kim et al., 2011b). Based on information collected with the BSID-II as part of the Hokkaido study of 328 mother–infant pairs, Minatoya et al. (2016) reported that maternal blood levels of DEHP between 23 and 41 weeks of gestation were not associated with mental or psychomotor development in children at 6 or 18 months (Minatoya et al., 2016). Based on measurements of CBCL from 430 mother–infant pairs in the TMICS analysis, Lien et al. (2015) reported a positive association between maternal urine DEHP and DBP levels during the third trimester and externalizing domain behavior problems in 8-year-old children (Lien et al., 2015).

6.3. Endocrine function and puberty

Based on information from the Hokkaido study of 328 mother–infant pairs, Minatoya et al. (2016) reported that maternal blood levels of MEHP between 23 and 41 weeks of gestation were not associated with thyroid hormone levels at 6 or 18 months (Minatoya et al., 2016). Data collected from 148 Taiwanese mother–infant pairs in Kaohsiung showed that maternal urine levels of MBzP in the third trimester were inversely associated with TSH levels in cord blood (Kuo et al., 2015).

TMICS published a series of studies investigating phthalate in relation to reproductive function and puberty. Lin et al. (2011) reported that maternal urine levels of DEHP during the third trimester were negatively correlated with free testosterone (fT) and fT/estrogen (E2) levels in cord blood (Lin et al., 2011). Secondly, they found that maternal urine levels of phthalate during the third trimester did not significantly alter birth outcomes, growth, or reproductive function or development in pre-pubertal children (8 years of age). The study also found that levels of phthalate metabolites (including MEHP, MnBP, and MBzP) in 8-year-old girls appear to correlate with serum levels of follicle-stimulating hormone (FSH) and progesterone (Su et al., 2014). Thirdly, they showed One study in children aged 8 or 11 years showed that elevated total DEHP, MBzP, and maternal phthalate levels during the third trimester may delay pubertal development for females but not males (Su et al., 2015a). In addition, inverse associations between maternal MEHP at 23–35 weeks of gestation and T/E2, progesterone, inhibin B, and insulin-like factor 3 (INSL3) were statistically significant for males' infant in cord blood. DEHP exposure in utero may have adverse effects on both Sertoli and Leydig cell development in males (Araki et al., 2014).

6.4. Allergic disease and immune function

Wang et al. (2014a) reported that maternal urine levels of MEHP during the third trimester were positively correlated with serum IgE levels. In addition, maternal urine MEHP levels during the third trimester were associated with atopic dermatitis at 2 years of age (Wang et al., 2014a). The TMICS group followed children at ages of 2, 5, and 8 years; samples were obtained from the mothers of those included in the study to measure levels of phthalate exposure. The authors found that higher maternal MBzP levels during the third trimester were associated with 5-fold increase in wheezing in boys and substantial increases in IgE levels in 8-year-old children of both sexes. Urinary MEHP levels at 2 years of age and DEHP levels at 5 years of age were associated with increased asthma occurrence in boys (Ku et al., 2015).

7. Perfluoroalkyl substances

Table 5 shows the association between PFAS, fetal growth and pregnancy outcomes, neurodevelopment and behavioral problems, endocrine function and puberty, and allergic disease and immune function. Birth weight was measured by two cohorts, and one cohort measured the growth from birth to childhood. Different neurodevelopment and behavioral questionnaires were used by different cohorts. Four cohorts measured the TSH and T4 for endocrine evaluation. Three cohorts used ISAAC questionnaire and two cohorts measured IgE levels for allergy and immune function.

7.1. Fetal growth and pregnancy outcome

In 2009, the Hokkaido study reported that maternal PFOS levels at 23–35 weeks of gestation were negatively correlated with neonatal birth weight (Washino et al., 2009). In 2015, the Study reported a negative association between maternal PFOS levels after the second trimester of pregnancy and birth weight, especially for female children, and an inverse association between PFOS exposure and polyunsaturated fatty acid levels in pregnant women (Kishi et al., 2015). In addition, TBPS reported an inverse association was observed between cord blood PFOS levels and birth outcomes (gestational age, birth weight, and head circumference) (Chen et al., 2012a). TMICS observed that long-chain perfluorocarboxylic acids (PFCA) levels at gestational weeks 37–42

Table 4
Association between phthalate and children's health outcomes.

Birth Cohort, Nationality	Year	Mother-infant	Exposure	Main outcome	Results	Association	Reference
Fetal growth and pregnancy outcome							
CHECK, Korea	2016	128	Maternal blood and urine before delivery, placenta, cord blood	BW, length and head circumference; weight and length 3 months after birth through a telephone interview; leptin, total cholesterol and TG in cord serum	Exposure to DEHP is associated with decrease of PI and increase of TG at birth. Body mass increase is accelerated in newborn infants exposed to DEHP.	PI: β = −0.11, p = 0.070; TG: β = 0.14, p = 0.027	Kim et al., 2016
Hokkaido, Japan	2017	167	Maternal blood at the third trimester	Birth size, adiponectin and leptin	MEHP were associated with cord blood PI.	β = −1.28 (CI −2.43 to −0.13)	Minatoya et al., 2017
Neurodevelopment and behavioral problems							
MOCEH, Korea	2011	460	Maternal urine during third trimester	BSID-II at 6 months of age	Prenatal Exposure to MEHHP, MEOHP and MBP were inversely associated with MDI and PDI of the BSID among 6-month-old male infants.	MDI-MEHHP: β = −0.97 (CI −1.85 to −0.08); MDI-MEOHP: β = −0.95 (CI −1.87 to −0.03); PDI-MEHHP: β = −0.93 (CI −1.82 to −0.05)	Kim et al., 2011b
TMICS, Taiwan	2015	122	Maternal urine during the third trimester, children's urine samples collected at 8–9 years of age.	CBCL at 8 years of age	Positive associations between maternal MEOHP exposure and externalizing domain behavior problems in 8-year-old children.	MEOHP: β = 3.74 (CI 1.33 to 6.15)	Lien et al., 2015
Hokkaido, Japan	2016	328	Maternal blood between 23 and 41 weeks of gestation	BSID-II at 6 and 18 month of age.	Prenatal MEHP exposure did not show adverse effects on mental and psychomotor development at 6 and 18 months of age.	No association	Minatoya et al., 2016
Endocrine function and puberty							
Kaohsiung, Taiwan	2015	148	Maternal urine at the third trimesters	Third trimester and cord blood TSH, T4, FT4, T3	Higher the urinary MBzP levels in pregnant mothers, the lower the TSH levels in cord blood serums.	β = −2.644, p = 0.003	Kuo et al., 2015
Hokkaido, Japan	2016	328	Maternal blood between 23 and 41 weeks of gestation	TSH and FT4	Prenatal DEHP exposure did not show adverse effects on infant thyroid hormone levels.	No association	Minatoya et al., 2016
TMICS, Taiwan	2011	155	Maternal urine in the third trimesters	Cord blood fT, E2	Maternal DEHP levels were negatively correlated with free testosterone (fT) and fT/E2 levels in cord blood in female.	fT: r = −0.38, p < 0.001;T/E2: r = −0.35, p < 0.01	Lin et al., 2011
Hokkaido, Japan	2014	514	Maternal blood from 23 to 35 weeks of gestation	Cord blood E2, T PG, INSL3, SHBG, FSH, LH, and inhibin B,	Inverse associations between maternal MEHP levels and T/E2, PG, and inhibin B were statistically significant for males. DEHP exposure in utero may have adverse effects on both Sertoli and Leydig cell development in males.	T/E2: β = −171 (CI −2.95 to −0.048); PG: β = −0.237 (CI −0.401 to −0.074); Inhibin B: β = −0.288 (CI −0.405 to −0.170)	Araki et al., 2014
TMICS, Taiwan	2014	130	Maternal urine in the third trimesters	T, fT, FSH, LH, E2, and PG at age of 8	Environmental exposure to certain phthalate metabolites (MEHP, MnBP, and MBzP) appears to correlate serum FSH and PG in pre-pubertal girls.	MEHP-PG: $\beta = 5.1 \times 10^{-4} \pm$ SE$1.2 \times 10^{-4;}$ MnBP-FSH: β = 0.26 ± SE0.0086; MBzP-FSH: β = 0.125 ± SE0.1726	Su et al., 2014
TMICS, Taiwan	2015	133	Maternal urine in the third trimesters	Bone age, chronological age, genital and armpit development, pelvic organ examination, Tanner stage, uterus sizes and ovarian volume at age of 8 and 11	Prenatal exposure to total DEHP and MBzP may delay the pubertal development for females but not for males.	Bone age: β = −0.07 (CI −0.13 to −0.01); Uterus size: β = −0.34 (CI −0.67 to −0.01)	Su et al., 2015a
Allergic disease and immune function							
TBPS, Taiwan	2014	161	Maternal urine at 3rd trimester, urine at age 2, 5	Cord blood IgE, ISAAC	Urine MEHP was positively correlated with serum IgE levels, and urine MBzP had a significant association with atopic dermatitis at 2 years of age.	MEHP-IgE β = 0.191, p = 0.02; MBzP- atopic dermatitis β = 0.256, p = 0.03	Wang et al., 2014a

(continued on next page)

Table 4 (*continued*)

Birth Cohort, Nationality	Year	Mother-infant	Exposure	Main outcome	Results	Association	Reference
TMICS, Taiwan	2015	171	Maternal urine in the third trimesters, urine at age 2, 5, 8	ISAAC, IgE at age 8	Higher maternal MBzP levels were associated with an approximately 5× increase in the odds of wheezing in boys and substantial increases in IgE levels in 8-year-old children of both sexes. Prenatal and postnatal exposure to phthalate was associated with the occurrence of asthma in children, particularly for boys.	MBzP-wheezing at 8: OR = 4.95 (CI 1.08 to 22.63); MEHP-asthma at 5: OR = 4.36 (CI 1.01 to 18.86)	Ku et al., 2015

Birth weight (BW), triglyceride (TG), Ponderal index (PI), Bayley Scales of Infant Development—second edition (BSID-II), Child Behavior Checklist (CBCL), free testosterone (fT), testosterone (T), estradiol (E2), luteinizing hormone (LH), follicle-stimulating hormone (FSH), thyroid stimulating hormone (TSH), free thyroxine (fT4), thyroxine (T4), triiodothyronine (T3), free triiodothyronine (fT3), progesterone (PG), insulin-like factor 3 (INSL3), steroid hormone-binding globulin (SHBG), International Study of Asthma and Allergies in Childhood (ISAAC).

may interfere with fetal birth weight and childhood height in girls, and with childhood height in boys (Wang et al., 2016).

7.2. Neurodevelopment and behavioral problems

TBPS reported that PFOS in cord blood may affect child development, especially gross-motor development at 2 years of age (Chen et al., 2013). Based on information gathered using the Swanson, Nolan, and Pelham IV scale (SNAP-IV), the CBCL, and the Strengths and Difficulties Questionnaire (SDQ), TBPS and TEC found that cord blood PFNA levels were associated with neurobehavioral symptoms related to ADHD among 7-year-old children. (Lien et al., 2016). Based on analysis of results obtained using the full-scale intelligence quotient (FSIQ), verbal IQ (VIQ) and performance IQ (PIQ) indices, TMICS observed that long-chain PFASs (PFUnDA and PFNA) were associated with decreased IQ test scores in 5- and 8-year-old children (Wang et al., 2015). Based on information obtained using the BSID-II, the Hokkaido study reported an inverse association between maternal PFOA levels after the second trimester and the scores of female children on scales of mental neurodevelopment at 6 months of age (Goudarzi et al., 2016b).

7.3. Endocrine function and puberty

In 2014, TMICS found that levels of PFASs during pregnancy may reflect lower levels of T3 and total T4 in pregnant women and fetuses (Wang et al., 2014b). In 2016, the Hokkaido study reported that maternal PFOS levels between 24 and 41 weeks of gestation were associated with decreased maternal TSH and increased infant TSH (Kato et al., 2016). The Ewha Birth & Growth Retrospective Cohort (EBGRC) showed that elevated cord blood PFPeA levels were associated with significantly increased T4 levels. Increased levels of PFPeA and perfluorohexane sulfonic acid (PFHxS) were significantly associated with increased T4 and T3 levels in both sexes; elevated PFNA levels were associated with significantly decreased TSH levels in newborn girls (Shah-Kulkarni et al., 2016). Recently, TBPS reported that cord blood PFOS levels were negatively associated with T4, and positively associated with TSH (Tsai et al., 2017).

The Hokkaido study measured reproductive hormones as well. The study found that maternal PFOS levels after the second trimester of pregnancy were positively associated with dehydroepiandrosterone (DHEA) levels and negatively associated with cortisol and cortisone levels in cord blood, whereas PFOA showed a negative association with DHEA levels (Goudarzi et al., 2017). The authors also reported positive associations between PFOS levels and E2, and between PFOA land inhibin B; they reported negative association between PFOS and T/E2, progesterone, and inhibin B. PFOS levels were negatively associated with levels of P4 and PRL in female infants (Itoh et al., 2016).

7.4. Allergic disease and immune function

TBPS found that PFOA and PFOS levels were positively correlated with IgE levels in cord blood, especially in boys (Wang et al., 2011). The Hokkaido study reported that maternal PFOA levels after the second trimester were negatively associated with cord blood IgE levels, but found no association between maternal PFOA or PFOS and infant disease in infants aged 18 months (Okada et al., 2012). However, information obtained with the Japanese version of the International Study of Asthma and Allergies in Childhood (ISAAC) Phase Three questionnaire showed that lower maternal PFTrDA levels decreased the risk that children would develop eczema at age 12–24 months, especially females (Okada et al., 2014). Moreover, higher maternal PFDoDa and PFTrDA levels were associated with higher risk for immunosuppressive effects related to allergy in 4-year-old children (Goudarzi et al., 2016a).

8. Discussion

Accumulating evidence has showed that exposure to environmental pollutants including ETS, mercury, PCB, phthalates, and PFAS may impact pregnant women and children in Asia. ETS may affect infant birth weight, children's neurodevelopment, and development of allergy; mercury and PCB may affect children's neurodevelopment; phthalate impacts endocrine function; PFAS may influence children's neurodevelopment, endocrine function and allergy.

Most studies on environmental pollutants that have been conducted in Asia have reported the association between ETS and infant growth, children's neurodevelopment and allergy disease. Studies published in western countries have found a significant inverse relationship between maternal ETS exposure and the risk of low birth weight, SGA, and preterm birth (Leonardi-Bee et al., 2011; Nieuwenhuijsen et al., 2013). Birth weight is a commonly used to evaluate infants at birth. Information can easily be obtained from the mother at her prenatal health visits. The present found ETS affected neurobehavior and allergy disease which were found the similar results from other areas (Cook and Strachan, 1997; Rauh et al., 2004; Burke et al., 2012; Polanska et al., 2015), but all reported from same cohorts with small sample size. Besides, limited evidence has been reported regarding ETS exposure as related to childhood growth and obesity in Asia. ETS may also influence developing endocrine system in children (Granger et al., 2007), though the issues remain to be investigated systematically in Asian countries. A symmetrical review reported the second-hand smoke exposure burden from 192 countries, there existed area diversity (Oberg et al., 2011). Due to different race and susceptibility, future studies must consider potential impacts of gene expression on these issues. Most studies investigating these topics use questionnaires to evaluate ETS exposure; however, the use of questionnaires may involve bias. Future research studies should incorporate the use of biomarker such as cotinine or nicotine. In addition, most Asia area's living environment is more crowded than that in western countries, and the combination of household pollutants

Table 5
Association between perfluoroalkyl substances (PFAS) and children's health outcomes.

Birth Cohort, Nationality	Year	Mother-infant	Exposure	Main outcome	Results	Association	Reference
Fetal growth and pregnancy outcome							
Hokkaido, Japan	2009	428	Maternal blood after second trimester	BW and birth size	In utero exposure to relatively low levels of PFOS was negatively correlated with BW.	β = −148.8 (CI −297 to −0.5)	Washino et al., 2009
TBPS, Taiwan	2012	429	Cord blood	GA, BW, birth length, head circumference, PI	An adverse dose-dependent association was observed between prenatal PFOS exposure and birth outcomes.	Gestational age: β = −0.37 (CI −0.60 to −0.13); Birth weight: β = −110.2 (CI −176 to −44.5); Birth length: β = −0.25 (CI −0.46 to −0.05)	Chen et al., 2012a
Hokkaido, Japan	2015	306	Maternal blood after second trimester	Maternal FA and TG, birth size	A negative association between maternal PFOS levels and female BW.	β = −186.6 (CI −363 to −9.8)	Kishi et al., 2015
Children growth							
TMICS, Taiwan	2016	223	Maternal blood in third trimester	Birth size, weight and height at age 2, 5, 8, 11	Prenatal exposure to long-chain PFCAs may interfere with fetal and childhood growth in girls, and childhood growth in boys.	PFUnDA-birth weight (girl): β = −0.06 (CI −0.11 to −0.01); PFUnDA – weight Z score (girl): β = −0.15 (CI −0.28 to −0.02)	Wang et al., 2016
Neurodevelopment and behavioral problems							
TBPS, Taiwan	2013	239	Cord blood	CDIIT at age 2	Prenatal exposure to PFOS may affect children's development, especially gross-motor development at 2 years of age.	β = −3.7 (CI −0.60 to −1.5)	Chen et al., 2013
TMICS, Taiwan	2015	120	Maternal blood in third trimester	WPPSI-R at age 5; Chinese version of WISC-III at age 8	Two prenatal PFAS exposure, both long-chain PFASs (PFUnDA or PFNA), in association with decreased IQ test scores in 5- and 8-year-old children.	PFUnDA-IO at 5: β = −1.6 (CI −3.0 to −0.2); PFNA-IO at 8: β = −2.1 (CI −3.9 to −0.2)	Wang et al., 2015
Hokkaido, Japan	2016	428	Maternal blood after second trimester	BSID-II at age 6 and 18 months	Prenatal PFOA exposure may affect female mental scales of neurodevelopment at 6 months of age	β = −0.296 (CI −11.96 to −0.682)	Goudarzi et al., 2016b
TBPS & TEC, Taiwan	2016	282	Cord blood	SNAP-IV, CBCL, and SDQ	Prenatal exposure to PFNA (but not PFOA, PFOS, or PFUA) was found to associate with neurobehavioral symptoms related to ADHD among 7-year-old children.	SNAP-IV-inattention: β = −2.11 (CI −3.99 to −0.23); SDQ-Hyperactivity/Inattention: β = −0.01 (CI −1.06 to −1.09)	Lien et al., 2016
Endocrine function and puberty							
TMICS, Taiwan	2014	116	Maternal blood in third trimester	Maternal and cord blood fT4, T4, T3, and TSH.	Some PFASs during pregnancy may interfere with thyroid hormone homeostasis (lower T3 and total T4) in pregnant women and fetuses.	PFDoDA-Maternal T4: β = −1.742 (CI −2.785 to −0.7); PFDoDA-cord blood T4: β = −1.920 (CI −3.345 to −0.495)	Wang et al., 2014b
Hokkaido, Japan	2016	392	Maternal blood after second trimester	Maternal blood between the 7th and 20th weeks of gestation and infant blood between 4 and 7 of TSH and fT4	PFOS may independently affect the secretion and balances of thyroid function: decreased maternal TSH and increased infant TSH.	β = 0.214, p < 0.001; β = 0.177, p = 0.001	Kato et al., 2016
Hokkaido, Japan	2016	189	Maternal blood after second trimester	E2, T, PG, inhibin B, INSL3, SHBG, FSH, and LH, and PRL	PFOA levels were positively associated with inhibin B levels in male infants. Significant inverse associations between PFOS levels and P4 and PRL levels in female infants.	PFOA-inhibin B in male: β = 0.197 (CI 0.009 to 0.6384); PFOS-PG in female: β = −0.552 (CI −0.894 to 0.210)	Itoh et al., 2016
Hokkaido, Japan	2016	185	Maternal blood after second trimester	Cord blood cortisol, cortisone, DHEA, and androstenedione	Prenatal PFOS exposure was negatively associated with cortisol and cortisone levels and positively associated with DHEA level, whereas PFOA showed a negative association with DHEA levels.	PFOS-DHEA: β = 1.33 (CI 0.17 to 1.82); PFOA-DHEA: β = −1.23 (CI −1.72 to 0.25)	Goudarzi et al., 2017
EBGRC, Korea	2016	279	Cord blood	Cord blood T3, T4, and TSH	PFPeA impacted on thyroid hormone in cord blood, especially for girls (PFNA).	PFPeA-T4: β = 0.27 (CI 0.04 to 0.49)	Shah-Kulkarni et al., 2016
TBPS,	2017	118	Cord	Cord blood TSH, T3, T4, fT4,	PFOS were associated with thyroid hormone	PFOS-T4:	Tsai et al.,

(continued on next page)

Table 5 (*continued*)

Birth Cohort, Nationality	Year	Mother-infant	Exposure	Main outcome	Results	Association	Reference
Taiwan			blood	fT3	in cord blood.	β = −0.458 (CI −10.916 to −0.001)	2017
Allergic disease and immune function							
TBPS, Taiwan	2011	244	Cord blood	IgE in cord blood and children at age 2, ISAAC	Prenatal PFOA and PFOS exposures were positively correlated with cord blood IgE levels.	PFOS: β = 0.134, p = 0.047; PFOA: β = 0.161, p = 0.017	Wang et al., 2011
Hokkaido, Japan	2012	343	Maternal blood after second trimester	IgE in cord blood, questionnaire at 18 months	Although cord blood IgE level decreased significantly with high maternal PFOA levels among female infants, no relationship was found between maternal PFOS and PFOA levels and infant allergies and infectious diseases at age in 18 months.	PFOA in female: β = −1.429 (CI −2.416 to −0.422)	Okada et al., 2012
Hokkaido, Japan	2014	2063	Maternal blood after second trimester	ISAAC at age 12–24 months	Lower prenatal exposure to PFTrDA may decrease the risk of developing eczema in early childhood (12–24 months old), only in female.	OR = 0.62 (CI0.45 to 0.86)	Okada et al., 2014
Hokkaido, Japan	2016	1558	Maternal blood after second trimester	ISAAC at age 4	Prenatal exposure to long-chain PFASs, such as PFDoDa and PFTrDA may have an immunosuppressive effect on allergic diseases in 4-year-old children.	PFDoDa: OR = 0.621 (CI 0.454 to 0.847); PFTrDA: OR = 0.712 (CI 0.524 to 0.966)	Goudarzi et al., 2016a

Birth weight (BW), gestational age (GA), fatty acid (FA), Ponderal index (PI), Wechsler Preschool and Primary Scale of Intelligence-Revised (WPPSI-R), Wechsler's Intelligence Scale for Children-III (WISC-III), Bayley Scales of Infant Development—second edition(BSID-II), Swanson, Nolan, and Pelham IV scale (SNAP-IV), Strengths and Difficulties Questionnaire (SDQ), Child Behavior Checklist (CBCL), free testosterone (fT), testosterone (T), estradiol (E2), luteinizing hormone (LH), follicle-stimulating hormone (FSH), thyroid stimulating hormone (TSH), free thyroxine (fT4), thyroxine (T4), triiodothyronine (T3), free triiodothyronine (fT3), progesterone (PG), insulin-like factor 3 (INSL3), steroid hormone-binding globulin (SHBG), prolactin (PRL), dehydroepiandrosterone (DHEA), International Study of Asthma and Allergies in Childhood (ISAAC).

would be also considered in the future. The information collected could allow us to design effective interventions to prevent ETS exposure from negatively impacting children in Asia.

Health effects on fetuses and children were related to birth outcomes and neurobehavioral problems due to recognition of development neurotoxins (Grandjean and Landrigan, 2006, 2014; Jurewicz and Hanke, 2008). The present study has explored that associations among mercury and birth outcomes and allergic disease, but the results were inconsistent. Furthermore, evidences regarding the association between mercury and health impact on endocrine function and puberty development are lacking. Besides, seafood and fish consumption are the major sources of mercury especially methylmercury (MeHg), which is reported in some studies to have positive effects on fetal and children development (Olsen et al., 2006; Starling et al., 2015). However, few studies have explored the effects of consuming various foods, and no studies investigated cooking methods and the source which may influence the mercury concentration in human and be paid attention in global (Bradley et al., 2017). Therefore, the benefits of essential fatty acids, and toxicity of chemical pollutants such as mercury and dioxin related compounds remain the scientific basis of advisories regarding the consumption of fish and cooking methods. In the future, the role of gene-environmental interactions in relation to dietary needs to be considered.

In the present study, we also found that PCB exposure may affect the children's neurodevelopment, behavior, birth outcomes and endocrine function; however, the evidence was limited and inconsistent. In the past, most studies focused on high levels of PCB exposure with sufficient evidences (Wigle et al., 2008); related studies are being published at an increasing rate. One study used information from birth cohort studies conducted in Europe to report the effects of PCB on birth weight (Govarts et al., 2012). A systematic review found that prenatal or postnatal PCB exposure had adverse effects on neurodevelopment and behavior in children, though the results were inconsistent (Berghuis et al., 2015). Previous studies have reported that postnatal and maternal levels of PCB were associated with allergy symptom in childhood (Gascon et al., 2013; Hansen et al., 2014). However, there is no sufficient evidence to conclude the results either in Asia nor other areas. Additional studies must be conducted to investigate the health effects of low PCB exposure, especially in vulnerable and general populations. Fish is also a major source of PCB exposure, so the influence of co-exposure to another contaminants or nutrient cannot be ignored in the further study.

Phthalate was associated with endocrine function, especially on reproductive function in the present study. A review article reported that phthalates were related to reproductive disorders in both men and women (Annamalai and Namasivayam, 2015). However, findings in the study were limited and based on the same birth cohort group. Moreover, evidences for birth outcomes, neurobehavioral development, physical growth, and puberty development were also limited and inconsistent (Vrijheid et al., 2016). Because of its EDC properties, phthalate may interfere with the children's endocrine system and impact development (Yang et al., 2006), which could negatively impact neurodevelopment. Moreover, longitudinal studies will be necessary to evaluate the effects of phthalate from pre-puberty stage are also needed for assess puberty development. Besides, phthalates are widely used not only in Asia but also in the world, and human may exposure to phthalate through ingestion, inhalation, and dermal contact (Zarean et al., 2016). Therefore, further research will be necessary to elucidate the effects of on pediatric health by human biomonitoring.

PFAS exhibit characteristics of POPs and EDC, so PFAS exposure in human was associated with effects on endocrine function, growth, neurodevelopment, and behavioral (Bach et al., 2015). In the present study, four groups published that PFAS interfered with the balance of thyroid hormone; however, the carbon chain of PFAS and exposure period were different. In addition, although some systematic evidences showed that prenatal PFAS exposures was associated with negative birth outcomes (Johnson et al., 2014), no association was reported (Bach et al., 2015). Limited and controversial evidences and no systematic review articles have evaluated the effects of PFAS on neurodevelopment and allergic disease until now. PFOA and PFOS have been reduced and eliminated by authority (US EPA, 2012); however, the long half-lives property and other PFAS may also influence

children's health on whole area (Rand and Mabury, 2017). Therefore, we need more evidence regarding long term health effects on puberty development, reproductive function, obesity, and metabolic syndrome. Same as phthalate, human biomonitoring will be important for PFAS to know the impact on children's health.

This study summarized the effects of ETS, mercury, PCB, phthalate, and PFAS on children's health on fetal and children growth, neurodevelopment, behavior problems, endocrine function, immune function, and allergy disease. Some important environmental pollutants including air pollutant, dioxin, pesticides, bisphenol A (BPA), polybrominated diphenyl ethers (PBDE), and metals other than mercury were excluded from the present study. Exposure to air pollutants was associated with negative birth outcomes (Zhao et al., 2015). Dioxin may impact children's neurodevelopment (Tran et al., 2016). BPA may affect neonatal health (Bae et al., 2017). PBDE may interfere with female reproductive function (Gao et al., 2016). Evidence is accumulating for the effects of these environmental pollutants on the health of children. However, some cohorts' sample size was small and most studies based on Eastern Asia area, so these studies were not solid enough to make conclusions for children in Asia. We need to encourage other cohorts in Asia to put more efforts on children's environmental health. Moreover, future studies can explore the effects of these environmental pollutants on children's health from birth cohort groups, especially for large-scale and national-wide birth cohort studies. For example, to improve children's environmental health, the Ministry of Environment in Japan established a nation-wide birth cohort study called the Japan Environment and Children's Study (JECS) (http://www.env.go.jp/en/chemi/hs/jecs/) in 2011. The Ministry of Environment in Korea established Korean CHildren's ENvironmental health Study (Ko-CHENS) (http://environmentforchild.modoo.at/) in 2015 to monitor children into adulthood using biological samples and questionnaires focused on environmental exposure. Moreover, the China National Birth Cohort (CNBC) was initiated in 2016 to examine the early-life environmental exposure and children's health. Therefore, to widen a variety of population and help decision makers design better chemical risk management strategies for children in Asia, national-wide birth cohort studies should be performed in Asia. The DOHaD theory has led to the establishment of several groups that explore the impact of various nutrients on pediatric health, such as the Growing Up in Singapore Towards healthy Outcomes (GUSTO) cohort study. The GUSTP cohort study recently found that maternal consumption of vegetables, fruits, and white rice during pregnancy was associated with lower risks for preterm birth and larger birth size (Chia et al., 2016). According to the summary evidence in the present study, environmental pollutants are related to food consumption (e.g., seafood and mercury measurements). In order to completely evaluate pediatric health, a birth cohort study must be conducted in Asia.

Moreover, no matter the exposure scenario or outcome measurements are pivotal parts of evaluation on children's environmental health. Most studies focused on a single association between exposure and health outcomes. The exposure sources and routes were all co-exposure, so understanding multi-pollutant exposures and using multivariate statistical approaches for the further studies is urgent. Although it makes more difficult to identify the caused effects, pathway and mechanism, it is necessary to realize complexity of investigating environmental hazards and mixtures in a real world. Then we can establish exposure models of risk and assignment for Asia children, and exposure management for governments in Asia. In addition to exposure, mother, infant and children's genetic susceptibility from womb to childhood even to tombstone for genomics, transcriptomics, proteomics and metabolomics are also the key factors to elucidate the all scenario and then to compare to western countries and differentiate the main difference. Therefore, validation, harmonization, and international collaboration are needed in Asia. State of art technologies might help us to discover the underlying mechanism.

Acknowledgements

This study was supported by grants from Ministry of Science and Technology (MOST-105-2314-B-002-048-MY2), Taiwan and the Environmental Medicine Collaboration Center (NTUH-103-A123, NTUH-104-A123, and NTUH-105-A123), National Taiwan University Hospital.

Conflict of interest

We declare that no conflict of interest regarding financial, consultant, institutional, and other relationships leading to bias included in this manuscript.

References

Agay-Shay, K., Martinez, D., Valvi, D., Garcia-Esteban, R., Basagana, X., Robinson, O., 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, 1030–1037.
Annamalai, J., Namasivayam, V., 2015. Endocrine disrupting chemicals in the atmosphere: their effects on humans and wildlife. Environ. Int. 76, 78–97.
Araki, A., Mitsui, T., Miyashita, C., Nakajima, T., Naito, H., Ito, S., et al., 2014. Association between maternal exposure to di(2-ethylhexyl) phthalate and reproductive hormone levels in fetal blood: the Hokkaido Study on environment and children's health. PLoS One 9, e109039.
Bach, C.C., Bech, B.H., Brix, N., Nohr, E.A., Bonde, J.P., Henriksen, T.B., 2015. Perfluoroalkyl and polyfluoroalkyl substances and human fetal growth: a systematic review. Crit. Rev. Toxicol. 45, 53–67.
Bae, S., Lim, Y.H., Lee, Y.A., Shin, C.H., Oh, S.Y., Hong, Y.C., 2017. Maternal urinary bisphenol a concentration during midterm pregnancy and children's blood pressure at age 4. Hypertension 69, 367–374.
Barker, D.J., Winter, P.D., Osmond, C., Margetts, B., Simmonds, S.J., 1989. Weight in infancy and death from ischaemic heart disease. Lancet 2, 577–580.
Berghuis, S.A., Bos, A.F., Sauer, P.J., Roze, E., 2015. Developmental neurotoxicity of persistent organic pollutants: an update on childhood outcome. Arch. Toxicol. 89, 687–709.
Bradley, M.A., Barst, B.D., Basu, N., 2017. A review of mercury bioavailability in humans and fish. Int. J. Environ. Res. Public Health 14.
Burke, H., Leonardi-Bee, J., Hashim, A., Pine-Abata, H., Chen, Y., Cook, D.G., et al., 2012. Prenatal and passive smoke exposure and incidence of asthma and wheeze: systematic review and meta-analysis. Pediatrics 129, 735–744.
Chen, M.L., Chen, J.S., Tang, C.L., Mao, I.F., 2008. The internal exposure of taiwanese to phthalate—an evidence of intensive use of plastic materials. Environ. Int. 34, 79–85.
Chen, M.H., Ha, E.H., Wen, T.W., Su, Y.N., Lien, G.W., Chen, C.Y., et al., 2012a. Perfluorinated compounds in umbilical cord blood and adverse birth outcomes. PLoS One 7, e42474.
Chen, C.H., Lee, Y.L., Wu, M.H., Chen, P.J., Wei, T.S., Wu, C.T., et al., 2012b. Environmental tobacco smoke and male sex modify the influence of IL-13 genetic variants on cord blood IgE levels. Pediatric Allergy and Immunology: Official Publication of the European Society of Pediatric Allergy and Immunology 23, 456–463.
Chen, C.H., Wen, H.J., Chen, P.C., Lin, S.J., Chiang, T.L., Hsieh, I.C., et al., 2012c. Prenatal and postnatal risk factors for infantile pneumonia in a representative birth cohort. Epidemiol. Infect. 140, 1277–1285.
Chen, M.H., Ha, E.H., Liao, H.F., Jeng, S.F., Su, Y.N., Wen, T.W., et al., 2013. Perfluorinated compound levels in cord blood and neurodevelopment at 2 years of age. Epidemiology 24, 800–808.
Chia, A.R., de Seymour, J.V., Colega, M., Chen, L.W., Chan, Y.H., Aris, I.M., et al., 2016. A vegetable, fruit, and white rice dietary pattern during pregnancy is associated with a lower risk of preterm birth and larger birth size in a multiethnic Asian cohort: the growing up in Singapore towards healthy outcomes (GUSTO) cohort study. Am. J. Clin. Nutr. 104, 1416–1423.
Cook, D.G., Strachan, D.P., 1997. Health effects of passive smoking. 3. Parental smoking and prevalence of respiratory symptoms and asthma in school age children. Thorax 52, 1081–1094.
Doi, H., Nishitani, S., Fujisawa, T.X., Nagai, T., Kakeyama, M., Maeda, T., et al., 2013. Prenatal exposure to a polychlorinated biphenyl (PCB) congener influences fixation duration on biological motion at 4-months-old: a preliminary study. PLoS One 8, e59196.
Gao, Y., Chen, L., Wang, C., Zhou, Y., Wang, Y., Zhang, Y., et al., 2016. Exposure to polybrominated diphenyl ethers and female reproductive function: a study in the production area of Shandong, China. Sci. Total Environ. 572, 9–15.
Gascon, M., Morales, E., Sunyer, J., Vrijheid, M., 2013. Effects of persistent organic pollutants on the developing respiratory and immune systems: a systematic review. Environ. Int. 52, 51–65.
Ginsberg, G., Hattis, D., Miller, R., Sonawane, B., 2004. Pediatric pharmacokinetic data: implications for environmental risk assessment for children. Pediatrics 113, 973–983.
Gossner, C.M., Schlundt, J., Ben Embarek, P., Hird, S., Lo-Fo-Wong, D., Beltran, J.J., et al., 2009. The melamine incident: implications for international food and feed safety. Environ. Health Perspect. 117, 1803–1808.
Goudarzi, H., Miyashita, C., Okada, E., Kashino, I., Kobayashi, S., Chen, C.J., et al., 2016a. Effects of prenatal exposure to perfluoroalkyl acids on prevalence ofallergic diseases among 4-year-old children. Environ. Int. 94, 124–132.
Goudarzi, H., Nakajima, S., Ikeno, T., Sasaki, S., Kobayashi, S., Miyashita, C., et al., 2016b. Prenatal exposure to perfluorinated chemicals and neurodevelopment in early infancy: the Hokkaido Study. Sci. Total Environ. 541, 1002–1010.

Goudarzi, H., Araki, A., Itoh, S., Sasaki, S., Miyashita, C., Mitsui, T., et al., 2017. The association of prenatal exposure to perfluorinated chemicals with glucocorticoid and androgenic hormones in cord blood samples: the Hokkaido Study. Environ. Health Perspect. 125, 111–118.
Govarts, E., Nieuwenhuijsen, M., Schoeters, G., Ballester, F., Bloemen, K., de Boer, M., 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, 162–170.
Grandjean, P., Landrigan, P.J., 2006. Developmental neurotoxicity of industrial chemicals. Lancet 368, 2167–2178.
Grandjean, P., Landrigan, P.J., 2014. Neurobehavioural effects of developmental toxicity. The Lancet Neurology 13, 330–338.
Granger, D.A., Blair, C., Willoughby, M., Kivlighan, K.T., Hibel, L.C., Fortunato, C.K., et al., 2007. Individual differences in salivary cortisol and alpha-amylase in mothers and their infants: relation to tobacco smoke exposure. Dev. Psychobiol. 49, 692–701.
Guo, B.Q., Cai, S.Z., Guo, J.L., Xu, J., Wu, W., Li, H., et al., 2013. Levels of prenatal mercury exposure and their relationships to neonatal anthropometry in Wujiang city, China. Environ. Pollut. 182, 184–189.
Hansen, S., Strom, M., Olsen, S.F., Maslova, E., Rantakokko, P., Kiviranta, H., et al., 2014. Maternal concentrations of persistent organochlorine pollutants and the risk of asthma in offspring: results from a prospective cohort with 20 years of follow-up. Environ. Health Perspect. 122, 93–99.
Heindel, J.J., Balbus, J., Birnbaum, L., Brune-Drisse, M.N., Grandjean, P., Gray, K., et al., 2015. Developmental origins of health and disease: integrating environmental influences. Endocrinology 156, 3416–3421.
Hisada, A., Shimodaira, K., Okai, T., Watanabe, K., Takemori, H., Takasuga, T., et al., 2013. Serum levels of hydroxylated PCBs, PCBs and thyroid hormone measures of Japanese pregnant women. Environ. Health Prev. Med. 18, 205–214.
Hisada, A., Shimodaira, K., Okai, T., Watanabe, K., Takemori, H., Takasuga, T., et al., 2014. Associations between levels of hydroxylated PCBs and PCBs in serum of pregnant women and blood thyroid hormone levels and body size of neonates. Int. J. Hyg. Environ. Health 217, 546–553.
Hsi, H.C., Jiang, C.B., Yang, T.H., Chien, L.C., 2014. The neurological effects of prenatal and postnatal mercury/methylmercury exposure on three-year-old children in Taiwan. Chemosphere 100, 71–76.
Hsieh, C.J., Liao, H.F., Wu, K.Y., Hsieh, W.S., Su, Y.N., Jeng, S.F., et al., 2008. Cyp1a1 ile462val and gstt1 modify the effect of cord blood cotinine on neurodevelopment at 2 years of age. Neurotoxicology 29, 839–845.
Hsieh, C.J., Jeng, S.F., Su, Y.N., Liao, H.F., Hsieh, W.S., Wu, K.Y., et al., 2010. Cyp1a1 modifies the effect of maternal exposure to environmental tobacco smoke on child behavior. Nicotine & Tobacco Research: Official Journal of the Society for Research on Nicotine and Tobacco 12, 1108–1117.
Hsieh, C.J., Jeng, S.F., Wu, K.Y., Su, Y.N., Liao, H.F., Hsieh, W.S., et al., 2011. Gstm1 modifies the effect of maternal exposure to environmental tobacco smoke on neonatal primitive reflexes. Nicotine & Tobacco Research: Official Journal of the Society for Research on Nicotine and Tobacco 13, 1114–1122.
Hu, X., Zheng, T., Cheng, Y., Holford, T., Lin, S., Leaderer, B., et al., 2015. Distributions of heavy metals in maternal and cord blood and the association with infant birth weight in China. The Journal of Reproductive Medicine 60, 21–29.
Hu, Y., Chen, L., Wang, C., Zhou, Y., Zhang, Y., Wang, Y., et al., 2016. Prenatal low-level mercury exposure and infant neurodevelopment at 12 months in rural northern China. Environ. Sci. Pollut. Res. Int. 23, 12050–12059.
Itoh, S., Araki, A., Mitsui, T., Miyashita, C., Goudarzi, H., Sasaki, S., et al., 2016. Association of perfluoroalkyl substances exposure in utero with reproductive hormone levels in cord blood in the Hokkaido Study on Environment and Children's Health. Environ. Int. 94, 51–59.
Jensen, A.A., Leffers, H., 2008. Emerging endocrine disrupters: perfluoroalkylated substances. Int. J. Androl. 31, 161–169.
Johnson, P.I., Sutton, P., Atchley, D.S., Koustas, E., Lam, J., Sen, S., 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, 1028–1039.
Jorde, L.B., Wooding, S.P., 2004. Genetic variation, classification and 'race'. Nat. Genet. 36, S28–33.
Jurewicz, J., Hanke, W., 2008. Prenatal and childhood exposure to pesticides and neurobehavioral development: review of epidemiological studies. Int. J. Occup. Med. Environ. Health 21, 121–132.
Kato, S., Itoh, S., Yuasa, M., Baba, T., Miyashita, C., Sasaki, S., et al., 2016. Association of perfluorinated chemical exposure in utero with maternal and infant thyroid hormone levels in the Sapporo cohort of Hokkaido Study on the Environment and Children's Health. Environ. Health Prev. Med. 21, 334–344.
Katsikantami, I., Sifakis, S., Tzatzarakis, M.N., Vakonaki, E., Kalantzi, O.I., Tsatsakis, A.M., et al., 2016. A global assessment of phthalates burden and related links to health effects. Environ. Int. 97, 212–236.
Kaufman, A.S., Kaufman, N.L., 1983. Kaufman Assessment Battery for Children Interpretive Manual. American Guidance Service, Circle Pines, MN.
Kim, B.M., Lee, B.E., Hong, Y.C., Park, H., Ha, M., Kim, Y.J., et al., 2011a. Mercury levels in maternal and cord blood and attained weight through the 24 months of life. Sci. Total Environ. 410–411, 26–33.
Kim, Y., Ha, E.H., Kim, E.J., Park, H., Ha, M., Kim, J.H., et al., 2011b. Prenatal exposure to phthalates and infant development at 6 months: prospective Mothers and Children's Environmental Health (MOCEH) study. Environ. Health Perspect. 119, 1495–1500.
Kim, S., Park, J., Kim, H.J., Lee, J.J., Choi, G., Choi, S., et al., 2013. Association between several persistent organic pollutants and thyroid hormone levels in serum among the pregnant women of Korea. Environ. Int. 59, 442–448.
Kim, S., Park, J., Kim, H.J., Lee, J.J., Choi, G., Choi, S., et al., 2015. Association between several persistent organic pollutants and thyroid hormone levels in cord blood serum and bloodspot of the newborn infants of Korea. PLoS One 10, e0125213.
Kim, J.H., Park, H., Lee, J., Cho, G., Choi, S., Choi, G., et al., 2016. Association of diethylhexyl phthalate with obesity-related markers and body mass change from birth to 3 months of age. J. Epidemiol. Community Health 70, 466–472.
Kishi, R., Nakajima, T., Goudarzi, H., Kobayashi, S., Sasaki, S., Okada, E., et al., 2015. The association of prenatal exposure to perfluorinated chemicals with maternal essential and long-chain polyunsaturated fatty acids during pregnancy and the birth weight of their offspring: the Hokkaido Study. Environ. Health Perspect. 123, 1038–1045.
Kishi, R.Z.J., Ha, E.H., Chen, P.C., Tian, Y., Xia, Y., Tsuchiya, K.J., Nakai, K., Kim, S., Hong, S.J., Hong, Y.C., Lee, J.R., Jan Mohamed, H.J.B., Parajuli, R.P., Adair, L.S., Chong, Y.S., Guo, Y.L., Wang, S.L., Nishijo, M., Kido, T., Tai, P.T., Nandasena, S., 2016. Birth Cohort Consortium of Asia (BICCA) — current and future perspectives. Epidemiology http://dx.doi.org/10.1097/EDE.0000000000000698 (accepted).
Ko, T.J., Tsai, L.Y., Chu, L.C., Yeh, S.J., Leung, C., Chen, C.Y., et al., 2014. Parental smoking during pregnancy and its association with low birth weight, small for gestational age, and preterm birth offspring: a birth cohort study. Pediatrics and Neonatology 55, 20–27.
Kobayashi, S., Sata, F., Sasaki, S., Braimoh, T.S., Araki, A., Miyashita, C., et al., 2016. Combined effects of AHR, CYP1A1, AND XRCC1 genotypes and prenatal maternal smoking on infant birth size: biomarker assessment in the Hokkaido Study. Reprod. Toxicol. 65, 295–306.
Ku, H.Y., Su, P.H., Wen, H.J., Sun, H.L., Wang, C.J., Chen, H.Y., et al., 2015. Prenatal and postnatal exposure to phthalate esters and asthma: a 9-year follow-up study of a Taiwanese birth cohort. PLoS One 10, e0123309.
Kuo, F.C., Su, S.W., Wu, C.F., Huang, M.C., Shiea, J., Chen, B.H., et al., 2015. Relationship of urinary phthalate metabolites with serum thyroid hormones in pregnant women and their newborns: a prospective birth cohort in Taiwan. PLoS One 10, e0123884.
Lee, B.E., Hong, Y.C., Park, H., Ha, M., Koo, B.S., Chang, N., et al., 2010. Interaction between GSTM1/GSTT1 polymorphism and blood mercury on birth weight. Environ. Health Perspect. 118, 437–443.
Lee, B.E., Hong, Y.C., Park, H., Ha, M., Kim, J.H., Chang, N., et al., 2011. Secondhand smoke exposure during pregnancy and infantile neurodevelopment. Environ. Res. 111, 539–544.
Leonardi-Bee, J., Britton, J., Venn, A., 2011. Secondhand smoke and adverse fetal outcomes in nonsmoking pregnant women: a meta-analysis. Pediatrics 127, 734–741.
Lien, Y.J., Ku, H.Y., Su, P.H., Chen, S.J., Chen, H.Y., Liao, P.C., et al., 2015. Prenatal exposure to phthalate esters and behavioral syndromes in children at 8 years of age: Taiwan Maternal and Infant Cohort Study. Environ. Health Perspect. 123, 95–100.
Lien, G.W., Huang, C.C., Shiu, J.S., Chen, M.H., Hsieh, W.S., Guo, Y.L., et al., 2016. Perfluoroalkyl substances in cord blood and attention deficit/hyperactivity disorder symptoms in seven-year-old children. Chemosphere 156, 118–127.
Lim, S.S., Vos, T., Flaxman, A.D., Danaei, G., Shibuya, K., Adair-Rohani, H., et al., 2012. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the global burden of disease study 2010. Lancet 380, 2224–2260.
Lin, L.C., Wang, S.L., Chang, Y.C., Huang, P.C., Cheng, J.T., Su, P.H., et al., 2011. Associations between maternal phthalate exposure and cord sex hormones in human infants. Chemosphere 83, 1192–1199.
Marek, R.F., Thorne, P.S., Wang, K., Dewall, J., Hornbuckle, K.C., 2013. PCBs and OH-PCBs in serum from children and mothers in urban and rural U.S. communities. Environ. Sci. Technol. 47, 3353–3361.
Minatoya, M., Naka Jima, S., Sasaki, S., Araki, A., Miyashita, C., Ikeno, T., et al., 2016. Effects of prenatal phthalate exposure on thyroid hormone levels, mental and psychomotor development of infants: the Hokkaido Study on Environment and Children's Health. Sci. Total Environ. 565, 1037–1043.
Minatoya, M., Araki, A., Miyashita, C., Sasaki, S., Goto, Y., Nakajima, T., et al., 2017. Prenatal di-2-ethylhexyl phthalate exposure and cord blood adipokine levels and birth size: the Hokkaido Study on Environment and Children's Health. Sci. Total Environ. 579, 606–611.
Miyake, Y., Tanaka, K., Yasutake, A., Sasaki, S., Hirota, Y., 2011. Lack of association of mercury with risk of wheeze and eczema in Japanese children: the Osaka Maternal and Child Health Study. Environ. Res. 111, 1180–1184.
Miyake, Y., Tanaka, K., Arakawa, M., 2013. Active and passive maternal smoking during pregnancy and birth outcomes: the Kyushu Okinawa Maternal and Child Health Study. BMC Pregnancy and Childbirth 13, 157.
Miyashita, C., Sasaki, S., Ikeno, T., Araki, A., Ito, S., Kajiwara, J., et al., 2015. Effects of in utero exposure to polychlorinated biphenyls, methylmercury, and polyunsaturated fatty acids on birth size. Sci. Total Environ. 533, 256–265.
Mukherjee, A., Sengupta, M.K., Hossain, M.A., Ahamed, S., Das, B., Nayak, B., et al., 2006. Arsenic contamination in groundwater: a global perspective with emphasis on the Asian scenario. J. Health Popul. Nutr. 24, 142–163.
Nakajima, S., Saijo, Y., Kato, S., Sasaki, S., Uno, A., Kanagami, N., et al., 2006. Effects of prenatal exposure to polychlorinated biphenyls and dioxins on mental and motor development in Japanese children at 6 months of age. Environ. Health Perspect. 114, 773–778.
Ng, S., Lin, C.C., Hwang, Y.H., Hsieh, W.S., Liao, H.F., Chen, P.C., 2013. Mercury, apoe, and children's neurodevelopment. Neurotoxicology 37, 85–92.
Ng, S., Lin, C.C., Jeng, S.F., Hwang, Y.H., Hsieh, W.S., Chen, P.C., 2015. Mercury, apoe, and child behavior. Chemosphere 120, 123–130.
Nieuwenhuijsen, M.J., Dadvand, P., Grellier, J., Martinez, D., Vrijheid, M., 2013. Environmental risk factors of pregnancy outcomes: a summary of recent meta-analyses of epidemiological studies. Environmental Health: A Global Access Science Source 12, 6.
Oberg, M., Jaakkola, M.S., Woodward, A., Peruga, A., Pruss-Ustun, A., 2011. Worldwide burden of disease from exposure to second-hand smoke: a retrospective analysis of data from 192 countries. Lancet 377, 139–146.

Okada, E., Sasaki, S., Saijo, Y., Washino, N., Miyashita, C., Kobayashi, S., et al., 2012. Prenatal exposure to perfluorinated chemicals and relationship with allergies and infectious diseases in infants. Environ. Res. 112, 118–125.
Okada, E., Sasaki, S., Kashino, I., Matsuura, H., Miyashita, C., Kobayashi, S., et al., 2014. Prenatal exposure to perfluoroalkyl acids and allergic diseases in early childhood. Environ. Int. 65, 127–134.
Olesen, B.W., 2004. International standards for the indoor environment. Indoor Air 14 (Suppl. 7), 18–26.
Olsen, S.F., Osterdal, M.L., Salvig, J.D., Kesmodel, U., Henriksen, T.B., Hedegaard, M., et al., 2006. Duration of pregnancy in relation to seafood intake during early and mid pregnancy: prospective cohort. Eur. J. Epidemiol. 21, 749–758.
Park, J.S., Petreas, M., Cohn, B.A., Cirillo, P.M., Factor-Litvak, P., 2009. Hydroxylated PCB metabolites (OH-PCBS) in archived serum from 1950–60s California mothers: a pilot study. Environ. Int. 35, 937–942.
Perera, F., Li, T.Y., Lin, C., Tang, D., 2012. Effects of prenatal polycyclic aromatic hydrocarbon exposure and environmental tobacco smoke on child IQ in a Chinese cohort. Environ. Res. 114, 40–46.
Polanska, K., Jurewicz, J., Hanke, W., 2015. Smoking and alcohol drinking during pregnancy as the risk factors for poor child neurodevelopment — a review of epidemiological studies. Int. J. Occup. Med. Environ. Health 28, 419–443.
Rand, A.A., Mabury, S.A., 2017. Is there a human health risk associated with indirect exposure to perfluoroalkyl carboxylates (PFCAs)? Toxicology 375, 28–36.
Rauh, V.A., Whyatt, R.M., Garfinkel, R., Andrews, H., Hoepner, L., Reyes, A., et al., 2004. Developmental effects of exposure to environmental tobacco smoke and material hardship among inner-city children. Neurotoxicol. Teratol. 26, 373–385.
Shah-Kulkarni, S., Kim, B.M., Hong, Y.C., Kim, H.S., Kwon, E.J., Park, H., et al., 2016. Prenatal exposure to perfluorinated compounds affects thyroid hormone levels in newborn girls. Environ. Int. 94, 607–613.
Sharma, B.M., Bharat, G.K., Tayal, S., Nizzetto, L., Larssen, T., 2014. The legal framework to manage chemical pollution in india and the lesson from the persistent organic pollutants (pops). Sci. Total Environ. 490, 733–747.
Starling, P., Charlton, K., McMahon, A.T., Lucas, C., 2015. Fish intake during pregnancy and foetal neurodevelopment—a systematic review of the evidence. Nutrients 7, 2001–2014.
Su, P.H., Huang, P.C., Lin, C.Y., Ying, T.H., Chen, J.Y., Wang, S.L., 2012. The effect of in utero exposure to dioxins and polychlorinated biphenyls on reproductive development in eight year-old children. Environ. Int. 39, 181–187.
Su, P.H., Chen, J.Y., Lin, C.Y., Chen, H.Y., Liao, P.C., Ying, T.H., et al., 2014. Sex steroid hormone levels and reproductive development of eight-year-old children following in utero and environmental exposure to phthalates. PLoS One 9, e102788.
Su, P.H., Chang, C.K., Lin, C.Y., Chen, H.Y., Liao, P.C., Hsiung, C.A., et al., 2015a. Prenatal exposure to phthalate ester and pubertal development in a birth cohort in central Taiwan: a 12-year follow-up study. Environ. Res. 136, 324–330.
Su, P.H., Chen, H.Y., Chen, S.J., Chen, J.Y., Liou, S.H., Wang, S.L., 2015b. Thyroid and growth hormone concentrations in 8-year-old children exposed in utero to dioxins and polychlorinated biphenyls. J. Toxicol. Sci. 40, 309–319.
Suzuki, K., Nakai, K., Sugawara, T., Nakamura, T., Ohba, T., Shimada, M., et al., 2010. Neurobehavioral effects of prenatal exposure to methylmercury and PCBs, and seafood intake: neonatal behavioral assessment scale results of Tohoku study of child development. Environ. Res. 110, 699–704.
Tanaka, K., Miyake, Y., Sasaki, S., Ohya, Y., Hirota, Y., Osaka, M., et al., 2008. Maternal smoking and environmental tobacco smoke exposure and the risk of allergic diseases in Japanese infants: the Osaka Maternal and Child Health Study. The Journal of Asthma: Official Journal of the Association for the Care of Asthma 45, 833–838.
Tanaka, K., Miyake, Y., Arakawa, M., 2012. Smoking and prevalence of allergic disorders in Japanese pregnant women: baseline data from the Kyushu Okinawa Maternal and Child Health Study. Environmental Health: A Global Access Science Source 11, 15.
Tatsuta, N., Nakai, K., Murata, K., Suzuki, K., Iwai-Shimada, M., Yaginuma-Sakurai, K., et al., 2012. Prenatal exposures to environmental chemicals and birth order as risk factors for child behavior problems. Environ. Res. 114, 47–52.
Tatsuta, N., Nakai, K., Murata, K., Suzuki, K., Iwai-Shimada, M., Kurokawa, N., et al., 2014. Impacts of prenatal exposures to polychlorinated biphenyls, methylmercury, and lead on intellectual ability of 42-month-old children in Japan. Environ. Res. 133, 321–326.
Tielsch, J.M., Katz, J., Thulasiraj, R.D., Coles, C.L., Sheeladevi, S., Yanik, E.L., et al., 2009. Exposure to indoor biomass fuel and tobacco smoke and risk of adverse reproductive outcomes, mortality, respiratory morbidity and growth among newborn infants in south India. Int. J. Epidemiol. 38, 1351–1363.
Tran, N.N., Pham, T.T., Ozawa, K., Nishijo, M., Nguyen, A.T., Tran, T.Q., et al., 2016. Impacts of perinatal dioxin exposure on motor coordination and higher cognitive development in Vietnamese preschool children: a five-year follow-up. PLoS One 11, e0147655.
Tsai, M.S., Lin, C.C., Chen, M.H., Hsieh, W.S., Chen, P.C., 2017. Perfluoroalkyl substances and thyroid hormones in cord blood. Environ. Pollut. 222, 543–548.
Tsuji, M., Aiko, Y., Kawamoto, T., Hachisuga, T., Kooriyama, C., Myoga, M., et al., 2013. Polychlorinated biphenyls (PCBs) decrease the placental syncytiotrophoblast volume and increase placental growth factor (PLGF) in the placenta of normal pregnancy. Placenta 34, 619–623.
US EPA, 2012. 2010/2015 PFOA Stewardship Program. US Environmental Protection Agency.
Vrijheid, M., Casas, M., Gascon, M., Valvi, D., Nieuwenhuijsen, M., 2016. Environmental pollutants and child health—a review of recent concerns. Int. J. Hyg. Environ. Health 219, 331–342.
Wang, T.M., Su, C.W., Liao, H.F., Lin, L.Y., Chou, K.S., Lin, S.H., 1998. The standardization of the comprehensive developmental inventory for infants and toddlers. Psychol Test 45, 19–46.
Wang, I.J., Hsieh, W.S., Wu, K.Y., Guo, Y.L., Hwang, Y.H., Jee, S.H., et al., 2008. Effect of gestational smoke exposure on atopic dermatitis in the offspring. Pediatric Allergy and Immunology: Official Publication of the European Society of Pediatric Allergy and Immunology 19, 580–586.
Wang, I.J., Chen, P.C., Hwang, K.C., 2009. Melamine and nephrolithiasis in children in Taiwan. N. Engl. J. Med. 360, 1157–1158.
Wang, I.J., Hsieh, W.S., Chen, C.Y., Fletcher, T., Lien, G.W., Chiang, H.L., et al., 2011. The effect of prenatal perfluorinated chemicals exposures on pediatric atopy. Environ. Res. 111, 785–791.
Wang, I.J., Lin, C.C., Lin, Y.J., Hsieh, W.S., Chen, P.C., 2014a. Early life phthalate exposure and atopic disorders in children: a prospective birth cohort study. Environ. Int. 62, 48–54.
Wang, Y., Rogan, W.J., Chen, P.C., Lien, G.W., Chen, H.Y., Tseng, Y.C., et al., 2014b. Association between maternal serum perfluoroalkyl substances during pregnancy and maternal and cord thyroid hormones: Taiwan maternal and infant cohort study. Environ. Health Perspect. 122, 529–534.
Wang, Y., Rogan, W.J., Chen, H.Y., Chen, P.C., Su, P.H., Chen, H.Y., et al., 2015. Prenatal exposure to perfluroalkyl substances and children's IQ: the Taiwan maternal and infant cohort study. Int. J. Hyg. Environ. Health 218, 639–644.
Wang, Y., Adgent, M., Su, P.H., Chen, H.Y., Chen, P.C., Hsiung, C.A., et al., 2016. Prenatal exposure to perfluorocarboxylic acids (PFCAs) and fetal and postnatal growth in the Taiwan maternal and infant cohort study. Environ. Health Perspect. 124, 1794–1800.
Washino, N., Saijo, Y., Sasaki, S., Kato, S., Ban, S., Konishi, K., et al., 2009. Correlations between prenatal exposure to perfluorinated chemicals and reduced fetal growth. Environ. Health Perspect. 117, 660–667.
Wigle, D.T., Arbuckle, T.E., Turner, M.C., Berube, A., Yang, Q., Liu, S., et al., 2008. Epidemiologic evidence of relationships between reproductive and child health outcomes and environmental chemical contaminants. Journal of Toxicology and Environmental Health Part B, Critical Reviews 11, 373–517.
Wu, T., Hu, Y., Chen, C., Yang, F., Li, Z., Fang, Z., et al., 2007. Passive smoking, metabolic gene polymorphisms, and infant birth weight in a prospective cohort study of Chinese women. Am. J. Epidemiol. 166, 313–322.
Wu, K., Xu, X., Liu, J., Guo, Y., Huo, X., 2011. In utero exposure to polychlorinated biphenyls and reduced neonatal physiological development from Guiyu, China. Ecotoxicol. Environ. Saf. 74, 2141–2147.
Xu, X., Chiung, Y.M., Lu, F., Qiu, S., Ji, M., Huo, X., 2015. Associations of cadmium, bisphenol a and polychlorinated biphenyl co-exposure in utero with placental gene expression and neonatal outcomes. Reprod. Toxicol. 52, 62–70.
Yang, M., Park, M.S., Lee, H.S., 2006. Endocrine disrupting chemicals: human exposure and health risks. Journal of Environmental Science and Health Part C, Environmental Carcinogenesis & Ecotoxicology Reviews 24, 183–224.
Yasumura, S., Hosoya, M., Yamashita, S., Kamiya, K., Abe, M., Akashi, M., et al., 2012. Study protocol for the Fukushima Health Management Survey. Journal of Epidemiology 22, 375–383.
Yila, T.A., Sasaki, S., Miyashita, C., Braimoh, T.S., Kashino, I., Kobayashi, S., et al., 2012. Effects of maternal 5,10-methylenetetrahydrofolate reductase C677T and a1298C polymorphisms and tobacco smoking on infant birth weight in a Japanese population. Journal of Epidemiology 22, 91–102.
Yoshimura, T., Kaneko, S., Hayabuchi, H., 2001. Sex ratio in offspring of those affected by dioxin and dioxin-like compounds: the Yusho, Seveso, and Yucheng incidents. Occup. Environ. Med. 58, 540–541.
Zarean, M., Keikha, M., Poursafa, P., Khalighinejad, P., Amin, M., Kelishadi, R., 2016. A systematic review on the adverse health effects of di-2-ethylhexyl phthalate. Environ. Sci. Pollut. Res. Int. 23, 24642–24693.
Zhao, N., Qiu, J., Zhang, Y., He, X., Zhou, M., Li, M., et al., 2015. Ambient air pollutant PM10 and risk of preterm birth in Lanzhou, China. Environ. Int. 76, 71–77.