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Review

Environmental pollutants and child health—A review of recent concerns

Martine Vrijheid[a,b,c,*], Maribel Casas[a,b,c], Mireia Gascon[a,b,c,d], Damaskini Valvi[a,b,c,e], Mark Nieuwenhuijsen[a,b,c]

[a] ISGlobal, Centre for Research in Environmental Epidemiology (CREAL), Barcelona, Spain
[b] Universitat Pompeu Fabra (UPF), Barcelona, Spain
[c] CIBER Epidemiología y Salud Pública (CIBERESP), Barcelona, Spain
[d] ISGlobal, Barcelona Centre for International Health Research (CRESIB), Hospital Clínic—Universitat de Barcelona, Barcelona, Spain
[e] Department of Environmental Health, Harvard T. H. Chan School of Public Health, Boston, MA, United States

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ABSTRACT

In recent years, many new studies have evaluated associations between environmental pollutants and child health. This review aims to provide a broad summary of this literature, comparing the state of epidemiological evidence for the effects of a wide range of environmental contaminants (air pollutants, heavy metals, organochlorine compounds, perfluoroalkyl substances, polybrominated diphenyl ethers, pesticides, phthalates and bisphenol A) on child health outcomes. The review addresses effects on foetal growth and prematurity, neurodevelopment, respiratory and immune health, and childhood growth and obesity.

Findings of recent prospective studies and meta-analyses have corroborated previous good evidence, often at lower exposure levels, for effects on foetal growth of air pollution and polychlorinated biphenyls (PCBs), for neurotoxic effects of lead, methylmercury, PCBs and organophosphate pesticides, and for respiratory health effects of air pollution. Moderate evidence has emerged for a potential role of environmental pollutants in attention deficit hyperactivity disorder and autism (lead, PCBs, air pollution), respiratory and immune health (dichlorodiphenyldichloroethylene – DDE – and PCBs), and obesity (DDE). In addition, there is now moderate evidence that certain chemicals of relatively recent concern may be associated with adverse child health outcomes, specifically perfluorooctanoate and foetal growth, and polybrominated diphenyl ethers and neurodevelopment. For other chemicals of recent concern, such as phthalates and bisphenol A, the literature is characterised by large inconsistencies preventing strong conclusions.

In conclusion, since most of the recent literature evaluates common exposures in the general population, and not particularly high exposure situations, this accumulating body of evidence suggests that the unborn and young child require more protection than is currently provided. Large, coordinated research efforts are needed to improve understanding of long-term effects of complex chemical mixtures.

1. Introduction

The foetus and infant have long been recognised as especially vulnerable to the effects of environmental agents that disrupt developmental processes, with possible lifelong consequences. In utero and early postnatal stressors, including environmental contaminant exposures, can permanently change the body's structure, physiology, and metabolism, predisposing individuals to the development of serious chronic pathologies later in life (e.g. cardiovascular, metabolic, respiratory, and neurodegenerative disease), a hypothesis grounded in the Developmental Origins of Health and Disease (DOHaD) paradigm for which there is a growing evidential basis (Heindel et al., 2015). Up to relatively recently, good epidemiological evidence for developmental effects of prenatal or early postnatal exposures was available only for a few pollutants; for example, sufficient evidence was reported for associations between air pollution and birth outcomes and respiratory health, lead and neurodevelopment, mercury and mental retardation, PCBs and birth weight and neurodevelopment, and organophosphate pesticides and neurodevelopment (Wigle et al., 2008; Stillerman et al.,

* Corresponding author at: Center for Research in Environmental Epidemiology (CREAL), Parc de Recerca Biomèdica de Barcelona—PRBB C. Doctor Aiguader, 88, 08003 Barcelona, Spain.
E-mail address: mvrijheid@creal.cat (M. Vrijheid).

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2008). Since then, there has been a rapid increase in studies focusing on pollutants of more recent concern, such as currently produced endocrine disruptors (Casas et al., 2013) and pesticides (Saillenfait et al., 2015), and on a wider range of health outcomes during childhood, including autism (Lyall et al., 2014), asthma (Gascon et al., 2013), and obesity (Tang-Péronard et al., 2011). In-depth reviews have evaluated recent evidence for specific exposure or outcome areas; however, none compare evidence for a wide range of contaminants and child health outcomes.

This review therefore aims to provide a broad summary of the literature comparing the state of epidemiological evidence for child health effects of a selection of common chemical exposures during early life, including outdoor air pollutants, toxic heavy metals (lead, mercury, cadmium, arsenic), organochlorine compounds (PCBs, dichlorodiphenyl-trichloroethane/dichloroethylene – DDT/DDE, hexachlorobenzene – HCB, dioxins), perfluoroalkyl substances (PFASs), polybrominated diphenyl ethers (PBDEs), currently used pesticides (particularly organophosphates), phthalates, and bisphenol A (BPA). Exposure to these chemicals is wide-spread globally, through air, water, and food contamination, and many consumer goods including plastics and cosmetics. We include four areas of child health: foetal growth and preterm birth, neurodevelopment, respiratory and immune health, and childhood growth and obesity. We do not include congenital malformation, genital or pubertal development, childhood cancers, or mortality related outcomes.

2. Methods

In order to provide a broad summary of the state of epidemiological evidence we based this review on recent systematic review articles and international meta-analyses where available. We primarily identified relevant literature using the PubMed search engine (National Library of Medicine). Search strategies included keywords for the various combinations of health outcome and environmental exposure).

Keywords for exposures were: air pollution; heavy metals; lead; mercury; cadmium; arsenic; persistent organic pollutants; organochlorine compounds (OCs); polychlorinated biphenyls (PCBs); dichlorodiphenyldichloroethylene (DDE); hexachlorobenzene (HCB); dioxin; perfluoroalkyl substances (PFCs); perfluorooctane sulfonate (PFOS); perfluorooctanoate (PFOA); polybrominated diphenyl ethers (PBDEs); pesticides; organophosphate; chlorpyrifos; pyrethroids; pththalates; bisphenol A (BPA).

Keywords for outcomes were: birth outcomes; birth weight; foetal growth; preterm birth; gestational duration; gestational length; 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.

We performed the last search on 1 September 2015. From the retrieved abstracts of each search combination we first identified systematic reviews and meta-analyses published between 2010 and 2015. Where multiple systematic review articles were available on the same topic we limited ourselves to the last or most relevant review(s) on the topic. We restricted ourselves to articles that included prenatal/maternal intra-uterine exposures or postnatal childhood exposures (0–18 years). We limited our review to evidence from cross-sectional, case-control and prospective population-based studies and to articles published in the English language.

For topics with no recent reviews or meta-analyses we carried out a search for original articles in the years 2010–2015; again, the same keywords were used. For topics with recent reviews we searched for original articles published after the existing review, using the above keyword combinations; such articles were only included if we considered them relevant to our classification of the evidence.

We classified strength of evidence for each combination of pollutant exposure group and outcome based on the following levels of evidence: “Good” evidence for an association: if multiple studies and meta-analyses gave consistent results; “Moderate” evidence of an association: if multiple studies reported associations, but with some inconsistencies; “Insufficient” evidence for an association: if there were few studies or substantial inconsistencies between multiple studies; “No” evidence: if there were no or very few studies.

3. Foetal growth and preterm birth

This review includes two pregnancy-related outcomes: foetal growth and preterm birth. Foetal growth is commonly measured as continuous weight at birth, as low (<2500 g) and very low (<1500 g) birth weight (possibly restricted to term births), or as small for gestational age (corresponding to a birth weight lower than the 10th percentile of a suitable sex- and gestational age–specific weight reference distribution) (Slama et al., 2014). Birth weight is correlated with health status later in life. Gestational duration corresponds to the time between the first day of the last menstrual period and birth. Preterm birth (below 37 completed gestational weeks) is the most frequently dichotomisation of gestational duration. Preterm birth is associated with strongly increased perinatal mortality and long-term morbidity (Slama et al., 2014).

3.1. Outdoor air pollution

The main outdoor air pollutants studied in epidemiological studies relate to traffic and industrial sources and include carbon monoxide (CO), nitrogen dioxide (NO_2), ozone (O_3), particulate matter (PM – including $PM_{2.5}$ and PM_{10}), polycyclic aromatic hydrocarbons (PAHs), and sulphur dioxide (SO_2). One decade ago, evidence for an effect of outdoor air pollution on preterm birth and foetal growth restriction was classified as limited (Wigle et al., 2008) as there were few and inconsistent findings. Systematic reviews in 2010 and 2011 concluded that findings for PM and foetal growth outcomes and SO_2 and preterm birth were most consistent (Bonzini et al., 2010; Shah et al., 2011). Since then, a strong evidence base has emerged from several meta-analyses for an association between air pollution, especially CO, NO_2, PM_{10} and $PM_{2.5}$, and greater risk of preterm birth and low birth weight (Stieb et al., 2012; Dadvand et al., 2013; Pedersen et al., 2013; Lai et al., 2013). For example, odds ratios for term low birth weight ranged from 1.03 per 10 $\mu g/m^3$ $PM_{2.5}$ in a study meta-analysing data from studies across the world (Dadvand et al., 2013) to 1.18 per 5 $\mu g/m^3$ $PM_{2.5}$ in a study pooling data from 14 longitudinal European birth cohorts (Pedersen et al., 2013). Results for O_3 and SO_2 were found to be less consistent for both outcomes (Stieb et al., 2012). Because of the consistency of evidence from recent large pooling and meta-analysis studies we classified evidence as “good” (Table 1).

3.2. Heavy metals

We focus on exposure to toxic heavy metals: lead, mercury, cadmium, and arsenic. Associations between lead and foetal growth and preterm birth were classified as limited by Wigle et al. (2008), whereas evidence for other metals was classified as inadequate. Since then, further studies have reported that low-level lead exposure (<10 $\mu g/dL$ maternal blood) can negatively influence foetal growth, including birth weight and length, and preterm birth (Gundacker et al., 2010; Zhu et al., 2010). For mercury exposure,

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