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Mini review

Early life exposure to air pollution: How bad is it?

Carl H. Backes[a,1], Timothy Nelin[b,1], Matthew W. Gorr[b], Loren E. Wold[a,b,c,*]

[a] Department of Pediatrics, The Ohio State University, Columbus, OH, United States
[b] Center for Cardiovascular and Pulmonary Research, The Research Institute at Nationwide Children's Hospital, Columbus, OH, United States
[c] Department of Physiology and Cell Biology, The Ohio State University, Columbus, OH, United States

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ABSTRACT

Increasing concentrations of air pollution have been shown to contribute to an enormity of adverse health outcomes worldwide, which have been observed in clinical, epidemiological, and animal studies as well as *in vitro* investigations. Recently, studies have shown that air pollution can affect the developing fetus *via* maternal exposure, resulting in preterm birth, low birth weight, growth restriction, and potentially adverse cardiovascular and respiratory outcomes. This review will provide a summary of the harmful effects of air pollution exposure on the developing fetus and infant, and suggest potential mechanisms to limit the exposure of pregnant mothers and infants to air pollution.

Contents

1. Introduction

Rapid industrial growth and economic expansion in developing countries contributes to numerous adverse health consequences of air pollution exposure, with evidence implicating particulate matter (PM; component of air pollution) as the chief perpetrator of harmful health outcomes (Agency, 2006). Epidemiological studies have shown an association between PM exposure and adverse health outcomes for the past decade, particularly related to adult cardiovascular morbidity and mortality (Brook et al., 2004; Pope et al., 2004; Sun et al., 2010). This review will explore the growing literature on the effects of air pollution on fetal and infant development, including effects on cardiopulmonary disease, low birth weight (LBW), intrauterine growth retardation (IUGR), and pre-term birth. Given the vulnerability of immature organ systems to outside influences, the developing fetus and neonate may be at

Abbreviations: AOR, adjusted odds ratio; DEP, diesel exhaust particles; CRP, C-reactive protein; GST1, glutathione S-transferase; IL-6, interleukin-6; IUGR, intrauterine growth restriction; LBW, low birth weight; NOx, oxides of nitrogen; OR, odds ratio; PM, particulate matter; PM0.1, ultrafine particles, diameter < 0.1 μm; PM2.5, fine particles, diameter < 2.5 μm; PM10, coarse particles, diameter 2.5–10 μm; RR, adjusted risk ratio; SES, socioeconomic status; SOX, oxides of sulfur.

* Corresponding author at: Center for Cardiovascular and Pulmonary Research, The Research Institute at Nationwide Children's Hospital, Department of Pediatrics, The Ohio State University, 575 Children's Crossroads, WB4135, Columbus, OH 43215. United States. Tel.: +1 614 355 5765; fax: +1 614 355 5725.
E-mail address: Loren.Wold@nationwidechildrens.org (L.E. Wold).
[1] Equal first authorship.

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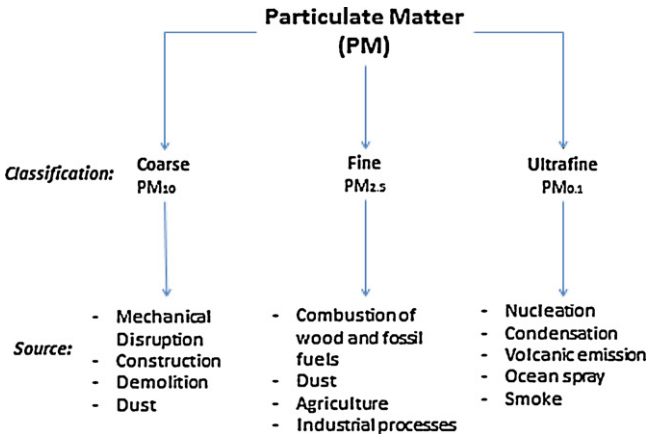

Fig. 1. PM represents a class of heterogeneous substances that exist as discrete particles, combining to form one component of air pollution. PM can be divided into three different categories based on size range: coarse, fine, and ultrafine. Both human and biogenic sources produce constituents of PM, and PM exposure has become a growing field for research as many adverse health consequences have been related to PM exposure.

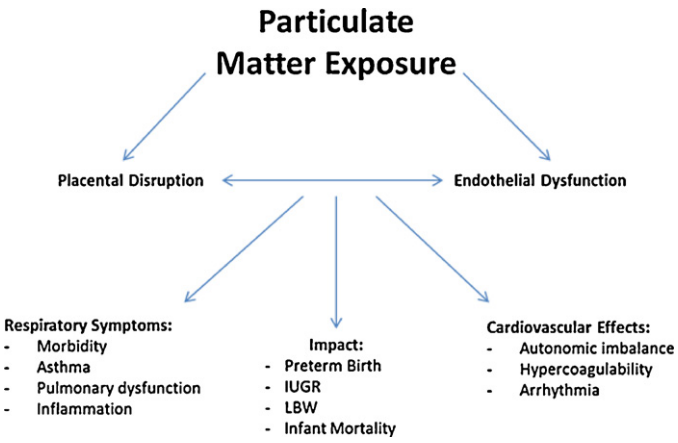

Fig. 2. PM is a major constituent of air pollution that is comprised of particles exhibiting three different size ranges. A number of cardiovascular effects have been related to increased levels of PM exposure. Studies have also demonstrated that fetal PM exposure may result in a host of developmental conditions including intrauterine growth restriction (IUGR), low birth weight (LBW), preterm birth, and infant mortality. The mechanisms of effect following PM exposure can be characterized by the onset of oxidative stress, which causes placental and endothelial dysfunction. This dysfunction can lead to the development of a number of cardiovascular and respiratory symptoms.

a greater risk for developing adverse health effects secondary to perinatal PM exposure (Choi et al., 2012; Pope, 2000). In addition, a longstanding line of evidence suggests that exposure to harmful levels of air pollutants accrued during sensitive periods of organ development may predispose an individual to developing certain adulthood cardiovascular pathologies (Bolton et al., 2012; Burton, 2009; Lacasana et al., 2005; Rocha et al., 2008; Sun et al., 2005).

This review will also focus on the potential impact of PM on pediatric outcomes, addressing vulnerabilities from fetal-life through infancy. Barker and Osmond (1986) initially proposed the concept that *in utero* variations in nutrient transfer from mother to child are related to LBW, ultimately resulting in adverse health outcomes later in life. Evidence detailed in this review expands upon this hypothesis, supporting the idea that environmental exposure to air pollution can similarly have harmful effects on the fetus. We aim to detail the harmful effects associated with fetal and infant PM exposure, and hopefully enhance international efforts to limit the exposure of pregnant mothers and children to PM and related air pollution sources.

2. PM sources and levels

Air pollution consists of a complex mixture of gases, liquids, and PM (Brook et al., 2004; Pope and Dockery, 2006). PM represents a diverse class of chemically and physically heterogeneous substances existing as separate particles (liquid droplets, solids, or semi-volatile materials) within the atmosphere (Agency, 2006). Human and biogenic sources emit PM into the ambient air, however human activity contributes the majority of primary PM present (Masih et al., 2010; Pandya et al., 2002; Wilhelm and Ritz, 2003). Motor vehicles, burning coal, residual oil, particles derived from the earth's crust, and forest fires produce constituents of PM (Nelin et al., 2012). Other activities contributing to increased PM concentrations in the ambient air include wood and fossil fuel combustion, industrial processes, indoor cooking with biofuels, construction, and demolition activities (Agency, 2005).

PM is normally expressed as the mass of particles within a cubic meter of air (micrograms per cubic meter, $\mu g/m^3$). PM in the ambient air contains three size ranges: coarse (PM 2.5–10 μm or PM_{10}), fine (PM < 2.5 μm or $PM_{2.5}$), and ultrafine (PM < 0.1 μm or $PM_{0.1}$) particles (Sun et al., 2010), as shown in Fig. 1. The present review focuses on $PM_{2.5}$, as it has been the main focus of many scientific and legislative efforts stemming from its well documented and reproducible negative effects on human health (Brook, 2008). Despite the focus on $PM_{2.5}$, it is critical to appreciate that particulate matter and air pollution exist as a heterogeneous mixture of gaseous and semi-volatile/volatile compounds, with biological toxicity based on the underlying chemical composition. This review also includes studies exploring constituents that contribute to air pollution, but are not classified as PM, such as NO_x, polycyclic aromatic hydrocarbons, SO_x, and tobacco smoke (Agency, 2006).

3. Adverse birth outcomes

The immature fetus is highly susceptible to toxicant exposure (Choi et al., 2012). This biological vulnerability is secondary to increased rates of cellular proliferation and growth, all in the setting of constantly changing metabolic and hormonal requirements. Any disruption in the efficiency of transplacental function *in utero* has the potential to negatively impact fetal growth and development, particularly during critical periods of organogenesis (Stevenson et al., 2003). Epidemiologic evidence suggests an association between PM_{10} and $PM_{2.5}$ exposure during pregnancy and adverse birth outcomes, including increased infant mortality, LBW, IUGR, and preterm birth (Bell et al., 2010b; Rossner et al., 2011; Rudra et al., 2011). Similar studies have demonstrated no association between fetal air pollution exposure and LBW, suggesting that the correlation between exposure and effect is delicate and might be enhanced by external factors such as region, SES, and duration of exposure (Rossner et al., 2011). A growing body of literature investigating the link between PM exposure and adverse perinatal outcomes has emerged due to the increasing potential of exposure to PM during pregnancy. Chronic exposure to air pollution may disrupt biological mechanisms that regulate fetal growth and development; however, current evidence suggests that particulate air pollution exposure can only be associated with minimal, at best, adverse effects on birth outcome (Glinianiaia et al., 2004). The specific mechanism(s) of this effect remain relatively unknown (Fig. 2). The effects of these and other clinical studies can be found in Table 1.