Establishing the exposure–outcome relation between airborne particulate matter and children's health

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With increasing urbanisation, industrialisation and economic growth worldwide, air pollution has emerged as one of the greatest global public health epidemics in the 21st century. The impacts of air pollution on human health are enormous. Globally, nine in ten people breathe air containing high levels of pollutants, and one in nine of the deaths are caused by exposure to air pollution, reaching an annual premature mortality of over seven million.[1] Air pollutants comprise a complex mixture of gases and particulate matter (PM), which are directly emitted from natural and anthropogenic sources or are formed in air via a multitude of chemical processes.[2] In particular, fine PM (diameter smaller than 2.5 µm or $PM_{2.5}$) has been unequivocally linked to various adverse human health effects, ranging from aggravated allergies to the development of chronic diseases, to premature death.[3] Exposure of vulnerable individuals to air pollution is especially worrisome, such as pregnant women and children.[4 5] The morbidity and mortality associated with air pollution for children are relevant to both prenatal and postnatal exposures. For example, epidemiological and animal model studies have revealed that maternal exposure to fine PM results in adverse birth outcomes and postnatal health conditions.[5] Specifically, animal model experiments employing ultrafine particles (diameter smaller than 0.1 µm or UFP) have shown that prenatal exposure predisposes offspring to long-term metabolic syndrome and pulmonary immunosuppression, with profound implications for respiratory infection risks.[6 7]

In this issue, Fang *et al*[8] assessed the impacts of UFP and $PM_{2.5}$ exposure on childhood respiratory diseases in Beijing, China. Time series of respiratory emergency room visits (ERVs) for children under 14 years old were collected between 2015 and 2017, during which period the city frequently experienced severe air pollution episodes.[9] The respiratory ERV data were correlated to concurrent measurements of size-fractioned PM number and mass concentrations from a close-to-traffic air quality monitoring station in Beijing using confounder-adjusted Poisson regression to determine the excessive risk (ER), and subgroup analyses were performed to evaluate cause-specific, age-specific and sex-specific effects as well as the linkage to the lag days after the exposure. The leading causes of ERVs included upper respiratory infections, bronchitis and pneumonia. Statistically significant correlations were identified between increased childhood respiratory morbidity and PM exposure. Among 136 925 ERV cases, an increased risk of all-respiratory ERVs was found to correlate with an IQR increase of UFPs (ER=5.4%; 95% CI 2.4% to 8.6%) and $PM_{2.5}$ (ER=1.3%; 95% CI 0.1% to 2.5%) at 0 and 1 prior days (lag0–1). Stronger effects were evident for children under 1 year old and for female sex. Additionally, source apportionment using positive matrix factorisation suggested that the dominant PM origins include nucleation (36.5%), gasoline vehicle emissions (27.9%), diesel vehicle emissions (18.9%) and secondary aerosols (10.6%). Significant associations of all-respiratory ERVs were found to be associated with secondary aerosols as well as emissions from gasoline and diesel vehicles, with increased ERs of 6.5% (CI 3.3% to 9.9%), 6.0% (CI 2.5% to 9.7%) and 4.4% (CI 1.7% to 7.1%) at lag0–1 days, respectively. In addition, exposures to other traffic-related pollutants (ie, black carbon and nitrogen dioxide) as well as particles in smaller sizes were also implicated to increased respiratory ERVs.

The findings by Fang *et al*[8] corroborate the previous studies on PM-exacerbated childhood respiratory risks.[10 11] Several parameters likely influence the health effects on children, including the amount and length of exposure (eg, the dose) as well as the PM properties (eg, size, number concentration, mass, chemical composition and toxicity). Specifically, inhaled particles contribute to oxidative stress and lung inflammation by releasing proinflammatory mediators or vasculoactive molecules from lung cells.[12] UFPs may be more lethal than $PM_{2.5}$ in inducing oxidative stress in macrophages and epithelial cells.[13] Particle size, surface area, redox capacity and ability to form radical species likely induce inflammatory effects, cause cellular DNA damage and inhibit the anti-inflammatory capacity of high-density lipoprotein in plasma and macrophage phagocytosis.[14] For example, the pattern for respiratory deposition onto the pulmonary tract is linked to particle size, and UFPs possess greater ability to penetrate deeper into the pulmonary region after inhalation.[6 7] Also, the insoluble fraction of UFPs is readily transmitted into the blood and circulates throughout the body, resulting in probably stronger adverse effects.[5] In addition, UFPs have a much shorter lifetime than $PM_{2.5}$ due to their efficient growth and coagulation removal in the atmosphere, corresponding to a much larger spatial and temporal variation.[15] Typically, UFPs are much less quantified in air quality monitoring,[2] and there exists a higher exposure misclassification for UFPs than $PM_{2.5}$.[5] Notably, available epidemiological studies on the health effects on children often produce inconsistent results concerning UFPs, and UFPs are currently unregulated in available ambient air quality standards.[5–7] Furthermore, combustion produces a large amount of polycyclic aromatic hydrocarbons,[16] which are also responsible for increased respiratory morbidity from traffic emissions.

Obtaining population health records is critical to accurate assessment and prediction of the adverse health effects of PM. The epidemiological and air quality data presented as well as the analyses conducted by Fang *et al*[8] represent an important step forward in accomplishing these objectives. On the other hand, major obstacles remain in elucidating PM-related morbidity and mortality in children, which are attributable to the complex biological mechanisms underlying adverse health effects and long-term outcomes, as well as deficiencies in understanding the sources and secondary formation of PM in air.[2 5] Notably, inadequate knowledge exists concerning differentiation between acute and chronic respiratory diseases as well as the adverse health effects due to maternal versus postnatal exposures. Another major challenge lies in the difficulty in entangling the complex

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interactions between the PM properties and the adverse health effects on children. Clearly, future research will need to characterise the sources, formation/transformation, spatial/temporal variabilities and toxicity for PM under different ambient conditions. Since traffic emissions represent one of the dominant sources of UFPs and $PM_{2.5}$ under urban environments,[17] it is imperative to establish the exposure–outcome relations from traffic-related pollutants in an age-specific and sex-specific fashion for the development of effective mitigation policies. Moreover, even in many developed countries (such as in the USA), low-income and minority populations are more likely to live closer to traffic-related pollution sources, and the combined vulnerabilities of exposure, race and social factors for children in underserved settings warrant special consideration.[5] Protecting vulnerable children from air pollution is paramount in policy decision-making, and achieving such a goal requires interdisciplinary studies in atmospheric, biological, medical, pathological and public health sciences.

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