Can Breathing Poor-quality Air Lead to Poor-quality Sleep in Children?

High-quality sleep is essential for child neurodevelopment, school performance, and general well-being. Unfortunately, sleep disorders are a common problem during childhood (1). In young children, sleep-disordered breathing and daytime sleepiness are more prevalent than are often recognized. Given the importance of healthy sleep for optimal child development, the identification of preventable risk factors is critical. Although there is evidence that exposure to air pollution is a risk factor for sleep-disordered breathing in adults (2), the published literature shows mixed results (3), leading to calls for more studies with a better assessment of air pollution exposures and objective measurement of sleep outcomes. In children, there is less available data about the impact of exposure to air pollution on sleep disturbances in general and sleep-disordered breathing in particular.

In this issue of the *Journal*, Cai and colleagues (pp. 602–612) report the results of a large population-based cohort of children aged 3–7 years recruited from 551 cities across China (4). Sleep quality was measured using the CSHQ (Children's Sleep Habits Questionnaire), and exposure to fine particulate matter ($PM_{2.5}$) was estimated using a validated satellite-based model. Early-life $PM_{2.5}$ exposure was associated with a higher total CSHQ score with a stronger association for postnatal exposure, especially for exposure during the first 18 months after birth, than exposure during pregnancy. Sleep-disordered breathing and daytime somnolence were the outcomes most strongly associated with postnatal $PM_{2.5}$ exposure. The investigators had a rich set of covariate data with which they could assess potential effect modification and found that children who were breastfed for less than 6 months and those who had been admitted to a neonatal ICU had significantly increased risk for sleep disturbances.

Although the study by Cai and colleagues was not the first to associate exposure to air pollution and sleep disturbances in children, it is the most definitive. In addition to the large national sample in China, the authors used a well-validated survey instrument to collect sleep quality data and had rich air pollution data, not only for $PM_{2.5}$ but also for other important air pollutants. With the air pollution exposure data, Cai and colleagues were able to fit two-pollutant models by adding SO_2, NO_2, CO, O_3, and coarse particulate matter ($PM_{2.5–10}$), respectively, into the model with $PM_{2.5}$ to examine possible confounding by coexposure to other air pollutants. As a sensitivity analysis, they also adjusted for the residential distance to major roadways as a proxy of traffic-related noise exposure in the model.

In brief, the study by Cai and colleagues provides evidence that both prenatal and postnatal exposure to $PM_{2.5}$ is associated with impaired sleep quality in preschool-aged children from a large, nationwide population in China. The study has multiple strengths, including the exploration of critical exposure windows for the adverse effects of $PM_{2.5}$ exposure on sleep health, including by trimester during pregnancy and during the first 36 months after birth. The authors used a validated satellite-based model to estimate $PM_{2.5}$ exposures with a high spatial-temporal resolution, which allowed coverage of areas disproportionally excluded from previous studies in China because of a lack of ground-level $PM_{2.5}$ monitoring data. The study population had sufficient variation in $PM_{2.5}$ exposure to enable investigation of the exposure–response relationship between $PM_{2.5}$ and sleep health across a range of exposures.

The study also had several limitations, including potential recall bias as a consequence of parental completion of the CSHQ, likely exposure misclassification because of lack of indoor air quality assessment and lack of data on child's time spent away from the residential address, and potential residual confounding from other residential characteristics. Caveats about the results of the study are that there was a high parental report of sleep disturbance in the study children, 76% on the basis of CSHQ score, and the relatively high mean $PM_{2.5}$ concentration, 55 $\mu g/m^3$, which potentially reduces the generalizability to areas with much lower concentrations of pollution. Despite these limitations, the study is a major contribution to the relatively scant published literature on exposure to air pollution and the risk of childhood sleep quality and disorders.

Exposure to $PM_{2.5}$ during early childhood has been associated with an array of adverse health effects, such as shorter telomere length (i.e., accelerated biological aging) (5), epigenetic modifications (6–8), gene expression changes (9), reduced somatic and lung function growth (10–12), altered brain development (13), and slower neurodevelopment (14). Although the mechanism of how $PM_{2.5}$ may affect sleep quality in children is not precisely known, it has been proposed that exposure may interrupt sleep through upper airway inflammation, leading to obstruction and central nervous system effects, including potential neuroinflammation (2, 15).

What is the takeaway message for providers of health care for children? During poor air quality episodes, such as those that occur in heavily polluted Asian cities or with wildfire smoke in Australia or the western United States, reduction of exposure by keeping children indoors with windows closed and using portable filtration devices should reduce the risk of impacts on sleep. And what is the message for air quality regulators and governmental leaders? Policies that reduce harmful emissions from traffic and power generation by moving economies away from fossil fuel combustion, as well as improved forest management to reduce the risk of catastrophic wildfires, will lower the risk of poor air quality episodes that harm children's health. ■

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Cancer or Not Cancer: That Is the Question

VOMIT syndrome (victim of modern imaging technology) has protean manifestations across the life of a patient, from chance findings on screening computed tomography scans in adults to antenatal fetal anomaly ultrasound scans. The antenatal discovery of a congenital thoracic malformation (CTM) on the midtrimester scan provokes anxiety, but the vast majority of CTMs regress in size as pregnancy progresses, and most such babies are completely well in the newborn period. The prevalence of postnatal complications in a previously asymptomatic CTM is debated, but the largest meta-analysis in more than 1,000 patients suggests a figure of less than 5% in the first two decades of life (1).

For the few individuals who are symptomatic, surgery is required, and then there is rarely a therapeutic dilemma. When complications occur, they are usually readily treatable, as with infection, bleeding, and pneumothorax. However, CTMs occasionally prove to be neoplasms *de novo*, such as pleuropulmonary blastoma, or may be malformations within which carcinomas arise. The real problem is, what advice should be offered to the parents of a completely well baby who is known to have a pathologically uncharacterized CTM? Although we have been wrestling with this for more than three decades, there is still no consensus.

In this issue of the *Journal*, Garinet and colleagues (pp. 615–619) report on the findings from excised CTMs from the large MALFPULM (Risk Factors of Neonatal Respiratory Distress for Newborns with Prenatally Diagnosed Congenital Lung Malformations) cohort, which has already given us valuable information about antenatal prognosis of CTMs (2, 3). The study was inevitably observational. There were 426 live-born infants with antenatal diagnoses of CTMs, of whom 285 underwent surgery in the first two years of life. Of these, the parents of 195 consented to genotyping, and oncogenes were identified in 18 excised specimens (9%; *KRAS* [*KRAS* proto-oncogene, GTPase], $n = 17$; *FGFR2* [fibroblast growth factor receptor 2], $n = 1$). Seven CTMs with mutations also had the surrounding, apparently healthy lung tissue examined, and in four, the same mutations were identified as in the areas of the malformations. However, whether mutations would have been present in uninvolved tissue throughout both lungs or only in the surrounding lobe is unclear and may be relevant to

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