Invited Commentary | Environmental Health

Adequate Prenatal Maternal Folate—An Additional Intervention Strategy Among Populations Affected by Prenatal Lead Exposure?

Marco Sanchez-Guerra, PhD, MSc; Andres Cardenas, PhD, MPH; Citlalli Osorio-Yañez, PhD, MSc

Barker and Osmond\(^1\) postulated that the prenatal and early life environment could program an individual’s health and disease risk. Mounting evidence now suggests that the prenatal environment plays a crucial role in health and development throughout the life course. Wang et al\(^2\) evaluated whether prenatal maternal lead exposure is associated with the intergenerational risk of overweight or obesity (OWO) and if adequate prenatal maternal folate levels are associated with a reduction of this risk. Leveraging data from the Boston Birth Cohort, a prospective, urban, low-income, US cohort, Wang et al\(^2\) reported that lead exposure in pregnancy remained a persistent problem in the United States, with lead detectable in all prenatal maternal blood samples.

This study by Wang et al\(^2\) observed a greater risk of OWO for children born to mothers with red blood cell (RBC) lead levels in the range of 2 to 4 μg/dL (odds ratio [OR], 1.35; 95% CI, 1.05-1.72) or of at least 5 μg/dL (OR, 1.65; 95% CI, 1.18-2.32) compared with prenatal maternal RBC lead levels of less than 2 μg/dL (to convert to micromoles per liter, multiply by 0.0483). In addition, children from mothers with OWO had the highest risk of OWO, with a 3-fold increase in the odds of OWO for children from mothers with prenatal RBC lead levels in the range of 2 to 4 μg/dL and a 4-fold increase in the odds of OWO for children of mothers with prenatal RBC lead levels of at least 5 μg/dL compared with children from mothers with no OWO and RBC lead levels of less than 2 μg/dL.

Interestingly, among mothers with OWO and RBC lead levels of at least 2 μg/dL, those who had adequate prenatal maternal plasma folate levels (> 9.0 ng/mL; to convert to nanomoles per liter, multiply by 2.266) had children with 41% lower odds of having OWO (OR, 0.59; 95% CI, 0.36-0.95) compared with mothers with OWO, RBC lead levels of at least 2 μg/dL, and lower plasma folate levels. Postnatal child RBC lead levels were not associated with childhood OWO independent of prenatal maternal RBC lead levels or prenatal maternal OWO status. These results highlight the prenatal period as a sensitive window for lead exposure.

It is calculated that approximately 140 000 new chemicals and pesticides have appeared since 1950 and that there is universal human exposure to approximately 5000 of those. However, less than half of them have been tested for safety or toxic effects.\(^3\) Moreover, their reproductive harm is poorly understood. Although some chemicals and their emissions have been restricted in an effort to decrease exposure, this has not been sufficient to reduce human harm from most chemicals. For instance, in the United States, lead was removed from gasoline in 1975, leading to lower lead exposure among the population and resulting in the current limit of 5 μg/dL for blood lead levels.\(^4\)

Unfortunately, it is now well recognized that there is no safe blood lead level, and it has been suggested that children, even if exposed to low doses of lead during fetal development, may have increased risk of disability, disease, and death in childhood or later in life.\(^3\) In fact, if the associations observed in the study by Wang et al\(^2\) are robust, it might suggest that the current obesity epidemic could be partly attributed to elevated lead exposures owing to an entire generation having been exposed to lead when it was commonly added to gasoline.

Obesity is a major worldwide public health concern. It has been estimated that OWO affects nearly 2 billion people and that 62% of the population with obesity are from low- and middle-income countries.\(^5\) Therefore, identifying preventable prenatal causes of obesity is a cornerstone in the fight against the obesity epidemic. Most research and recommendations for prevention have focused on modifying diet and physical activity. However, environmental factors during pregnancy could play a

Open Access. This is an open access article distributed under the terms of the CC-BY License.
key role in childhood obesity, as the data from Wang et al\(^2\) suggest. Unfortunately, mothers and children are continuing to be exposed to lead at a wide range of levels because of historical and contemporary practices. Therefore, continuous monitoring of blood lead levels, especially among pregnant women and in low-income communities, should be considered by governments and health care professionals as a routine test to reduce lead exposure. In addition, the study by Wang et al\(^2\) highlights the need to maintain adequate folate intake during pregnancy, not just to reduce the risk of neural tube defects among newborns\(^6\) but also to potentially protect children from the obesogenic action of prenatal lead exposure. Although the study by Wang et al\(^2\) suggested that adequate maternal folate levels might prevent OWO associated with lead, women who are planning to become or capable of becoming pregnant should follow the recommended guidelines for folate supplementation.\(^6\)

The study by Wang et al\(^2\) opens the door to new questions about whether adequate folate intake might modify the adverse effects of other chemical exposures. For example, previous studies have suggested that folate intake might protect against the health effects associated with air pollution exposure.\(^7,8\) Therefore, adequate folate intake might be used as prevention against the effects of air pollution in addition to policies that decrease exposure to these toxicants. These efforts could yield substantial public health benefits and represent novel tools in fighting the obesity epidemic. In addition, interventions could be directed to pregnant women in low-income communities who are the most affected by pollution and might lack adequate folate supplementation.\(^3\)

Lastly, the study by Wang et al\(^2\) raises the possibility that prenatal lead exposure might program postnatal levels of leptin and insulin, mediating the observed association with childhood OWO. As the authors suggested, epigenetic programming mechanisms might be involved. Future studies should evaluate if epigenetic markers established during early fetal development could be involved in increasing leptin and adiponectin levels and eventually leading to OWO in childhood.

These findings reinforce current efforts not only to decrease environmental exposures to human toxicants during the prenatal period but also to reduce global pollutant levels, leading to a healthier generation. In addition, adequate prenatal folate levels might serve as a complementary intervention strategy among populations affected by lead exposure. However, studies involving diverse groups in other environments are needed to confirm these findings. Future mechanistic studies should investigate if epigenetic mechanisms are involved in the metabolic programming of OWO associated with prenatal lead exposure.


