HEI STATEMENT

Synopsis of Research Report 237

Exploring the Link Between Early Life Air Pollution Exposures and the Infant Microbiome and Metabolome

BACKGROUND

Several studies have linked early-life environmental exposures, such as outdoor air pollution, to body mass index and overweight status in children, which are well-known risk factors for long-term adverse health outcomes, including heart disease and diabetes. The biological mechanisms underlying this relationship are not well understood, but recent research has suggested that air pollution exposures might contribute to obesity and other adverse outcomes through changes in the gut microbiome (the microbiota, including bacteria, fungi, viruses, and their genes, found in the human gastrointestinal tract) and their byproducts in the fecal metabolome (the collection of small molecules found in feces) (**Statement Figure**).

In response to HEI's *Request for Applications 18-2*: Walter A. Rosenblith New Investigator Award, Dr. Tanya Alderete of Johns Hopkins University submitted an application to HEI titled "Air Pollutants and the Gut Microbiota and Metabolome During Early Life: Implications for Childhood Obesity." Dr. Alderete proposed to examine whether prenatal and postnatal outdoor air pollution exposures, including traffic-related air pollution, can change infant gut bacteria and fecal metabolites. Such changes might alter infant growth trajectories in the first 2 years of life — a finding that could potentially provide new insights into the biological mechanisms through which air pollution might contribute to obesity.

APPROACH

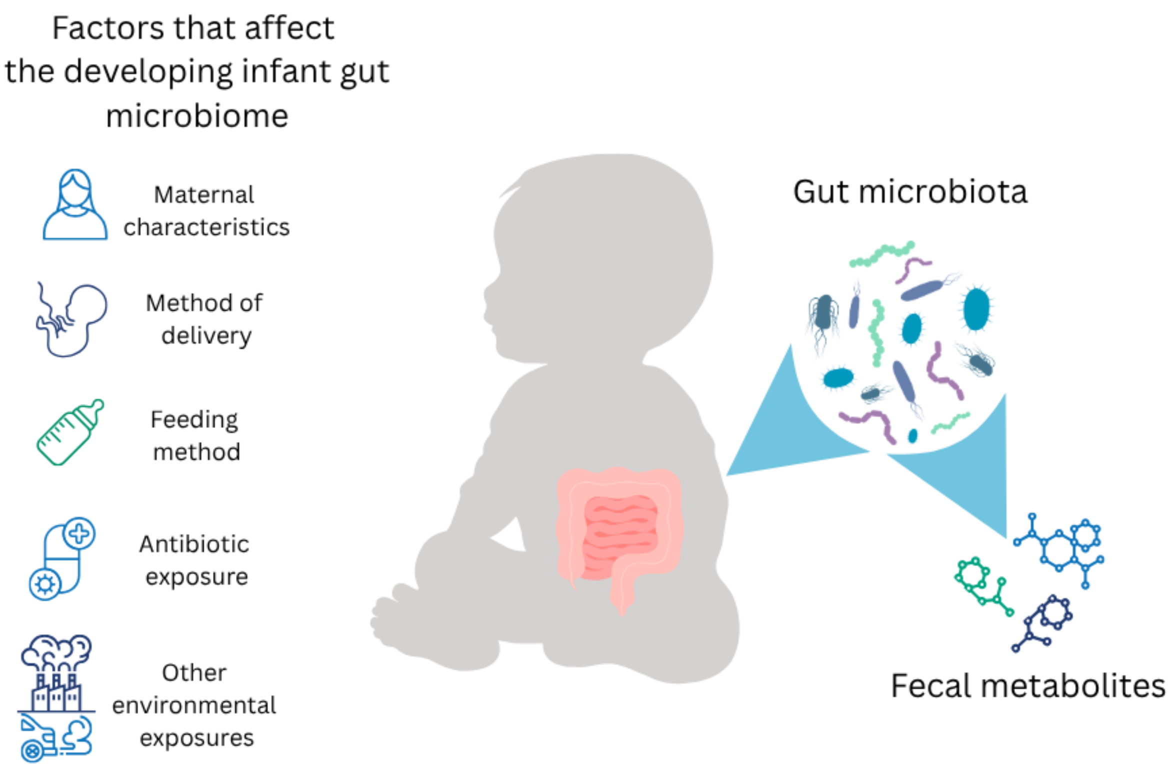
Dr. Alderete aimed to determine whether prenatal or postnatal exposure to air pollution is associated with a) lower diversity and altered relative abundances of gut bacteria and b) levels of specific fecal metabolites. She measured these endpoints at 1, 6, 12, 18, and 24 months after birth (Aim 1) and averaged these endpoints up to 24 months (Aim 2).

What This Study Adds

- This study examined whether prenatal or postnatal exposures to air pollution were associated with changes in the infant gut microbiome and fecal metabolome during the first 2 years of life.
- The team used a unique dataset of infant gut microbiota and fecal metabolites from a cohort of Hispanic mother–infant pairs in Southern California.
- Prenatal and postnatal air pollution exposures were associated with changes in the abundances of gut bacteria and levels of several fecal metabolites in infants during the first 2 years of life.
- Among participants with higher air pollution exposures, the team found some evidence of fewer beneficial gut bacteria, more potentially detrimental gut bacteria, and higher levels of metabolites indicative of oxidative stress and inflammation.
- This study provides a comprehensive set of exploratory analyses that contribute to our understanding of the relationships between air pollution and the infant gut microbiome and fecal metabolome.

Alderete and colleagues used a study cohort of 219 Hispanic mother–infant pairs participating in the Southern California Mother's Milk Study. Participants were enrolled at 1 month after birth and made several clinical visits up to 24 months after birth. The cohort included detailed information on the mother (such as age and socioeconomic status) and the infant (what their sex was, whether they were fed with human milk or formula, and when they started eating solid food). At each clinical visit, an infant stool sample was collected. Gut microbiome data were obtained from 207 infants, and fecal metabolome data were obtained from a subset of 127 infants. Stool samples were processed and analyzed using standard DNA sequencing and chemical analysis techniques.

This Statement, prepared by the Health Effects Institute, summarizes a research project funded by HEI and conducted by Dr. Tanya L. Alderete at Johns Hopkins Bloomberg School of Public Health in Baltimore, Maryland, and colleagues. Research Report 237 contains the detailed Investigators' Report and a Commentary on the study prepared by the HEI Review Committee.



Statement Figure. Overview of infant gut microbiome and fecal metabolome.

Based on the mothers' residential address histories, the team estimated prenatal and postnatal exposures to coarse particulate matter, fine particulate matter, nitrogen dioxide, ozone, and nitrogen oxides (a proxy for traffic-related air pollution) for each mother–infant pair. Prenatal exposure was based on the average of monthly air pollution exposure for the 9 months before birth. Postnatal exposure was based on air pollution exposures over short-term and long-term periods. Both prenatal and postnatal exposures were estimated using monthly concentrations of outdoor air pollutants derived from government monitoring data. Monthly traffic-related air pollution levels (nitrogen oxides) were estimated using an atmospheric dispersion model.

Alderete and colleagues used a combination of statistical models to evaluate associations between air pollution exposures and several outcomes of interest, including abundance (relative proportion of different types) and diversity (number of different types and distribution) of gut bacteria, as well as the identity and level of fecal metabolites.

KEY RESULTS

Gut Bacterial Abundance Alderete and colleagues reported that prenatal and postnatal exposures to several air pollutants were associated with short-term and long-term changes in the abundances of different gut bacteria. For instance, at various time points in early life, higher levels of prenatal exposure to coarse particulate matter, nitrogen dioxide, and nitrogen oxides were associated with a lower abundance of the beneficial gut bacterium *Bifidobacterium*. They also found that higher levels of prenatal exposure to nitrogen oxides were associated with a higher abundance of the potentially detrimental gut bacterium *Lelliottia amnigena*. In general, however, there were no clear trends or patterns across timepoints, specific gut bacterial abundances, or pollutant exposures.

Gut Bacterial Diversity Some postnatal air pollution exposures were associated with either increased or decreased diversity of gut bacteria, depending on infant age and the pollutant examined. For example, higher postnatal coarse particulate matter exposure was associated with greater gut bacterial diversity at 1 month after birth, whereas higher nitrogen oxide exposure was associated with reduced diversity at 6 months of age. More broadly, fewer associations were observed for diversity compared with gut bacterial abundance.

Fecal Metabolites The investigators found that exposures to coarse and fine particulate matter and nitrogen dioxide were associated with levels of several fecal metabolites at specific timepoints and altered levels over time up to 2 years. For instance, higher prenatal and postnatal exposures to fine particulate matter were associated with lower average levels of metabolites involved in histidine metabolism during the first 2 years of life — a finding that potentially indicates gut inflammation. However, there was no overlap in metabolite levels across pollutants.

INTERPRETATION AND CONCLUSIONS

In its independent review of the study, the HEI Review Committee concluded that this research provides a set of exploratory analyses investigating potential mechanistic links between air pollution and the gut microbiome and fecal metabolome in infants, with possible implications for childhood obesity.

Alderete and colleagues found that estimated prenatal and postnatal exposures to outdoor air pollution were associated with lower abundances of some beneficial species of gut bacteria, higher abundances of certain detrimental species of gut bacteria, and metabolites that indicate oxidative stress or gut inflammation. However, no clear patterns were evident across pollutants, timepoints, or outcomes examined.

The Committee identified the collection of a unique dataset on the infant gut microbiome and fecal metabolome, along with analyses at multiple timepoints after birth, as key strengths of the study. However, the Committee noted that the small size of the study cohort limits statistical power and, thus, the reliability of the results. Future studies could expand the scope by analyzing the current dataset for other microbiota, such as fungi and viruses, and by considering additional functional characteristics of the gut microbiota.