Air pollution alters immune function, worsens asthma symptoms

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Exposure to dirty air is linked to decreased function of a gene that appears to increase the severity of asthma in children, according to a joint study by researchers at Stanford University and the University of California, Berkeley.

While air pollution is known to be a source of immediate inflammation, this new study provides one of the first pieces of direct evidence that explains how some ambient air pollutants could have long-term effects.

The findings, published in the October 2010 issue of the *Journal of Allergy and Clinical Immunology,* come from a study of 181 children with and without asthma in the California cities of Fresno and Palo Alto.

The researchers found that air pollution exposure suppressed the immune system's regulatory T cells (Treg), and that the decreased level of Treg function was linked to greater severity of asthma symptoms and lower lung capacity. Treg cells are responsible for putting the brakes on the immune system so that it doesn't react to non-pathogenic substances in the body that are associated with allergy and asthma. When Treg function is low, the cells fail to block the inflammatory responses that are the hallmark of asthma symptoms.

The findings have potential implications for altered birth outcomes associated with polluted air, much the same as those noted for the effects of cigarette smoke.

"When it came out that cigarettes can cause molecular changes, it meant the possibility that mothers who smoked could affect the DNA of their children during fetal development," said study lead author Dr. Kari Nadeau, pediatrician at Stanford's Lucile Packard Children's Hospital and an assistant professor of allergy and immunology at Stanford's School of Medicine. "Similarly, these new findings suggest the possibility of an inheritable effect from environmental pollution."

Forty-one participants came from the Fresno Asthmatic Children's Environment Study (FACES), a longitudinal study led by principal investigator Dr. Ira Tager, professor of epidemiology at UC Berkeley's School of Public Health, and co-principal investigator S. Katharine Hammond, UC Berkeley professor and chair of environmental health sciences. The researchers also recruited 30 children from Fresno who did not have asthma.

"I'm not aware of any other studies that have looked at how chemicals can alter cells so early in the regulatory process, and then connected that effect to clinical symptoms," said Tager. "There are people who still question the direct link between air pollution and human health, but these findings make the health impact of pollutants harder to deny."

Fresno was chosen because it is located in California's Central Valley, where trapped hot air mixes with high traffic and heavy agriculture to create some of the highest levels of air pollution in the country. It is also a region known for its high incidence of asthma: Nearly one in three children there have the condition, earning Fresno the nickname, "The Asthma Capitol of California."

The researchers compared the participants from Fresno with 80 children, half with asthma and half without, in the relatively low-pollution city of Palo Alto, Calif. The children were matched by age, gender and asthma status, among other variables. The children were tested for breathing

function, allergic sensitivity and Treg cells in the blood.

Daily air quality data came from California Air Resources Board monitoring stations. The researchers calculated each child's annual average exposure to polycyclic aromatic hydrocarbons (PAH), a byproduct of fossil fuel and a major pollutant in vehicle exhaust.

The study found that the annual average exposure to PAH was 7 times greater for the children in Fresno compared with the kids in Palo Alto. Levels of ozone and particulate matter were also significantly higher in Fresno.

Not surprisingly, the study found that the children in Fresno had lower overall levels of Treg function and more severe symptoms of asthma than the children in Palo Alto. For example, the non-asthmatic children in Fresno had Treg function results that were similar to the children with asthma in Palo Alto.

The study authors correlated increased exposure to PAH with methylation of the gene, Forkhead box transcription factor (Foxp3), which triggers Treg cell development. Methylation effectively disables the gene's function, leading to reduced levels of Treg cells. The connection between Treg function and the severity of asthma symptoms held for children in both groups.

While previous studies have found associations between pollution – especially motor vehicle exhaust – and an increased risk of developing asthma, few have traced its molecular pathway so completely, the study authors said.

"The link between diesel exhaust and asthma could simply have been that the particulates were irritating the lungs," said Nadeau. "What we found is that the problems are more systemic. This is one of the few

papers to have linked from A to Z the increased exposure to ambient air pollution with suppressed Treg cell levels, changes in a key gene and increased severity of asthma symptoms."

The researchers noted that Treg cells are important for other autoimmune disorders, so the implications of this study could go beyond asthma.

Provided by University of California -- Berkeley