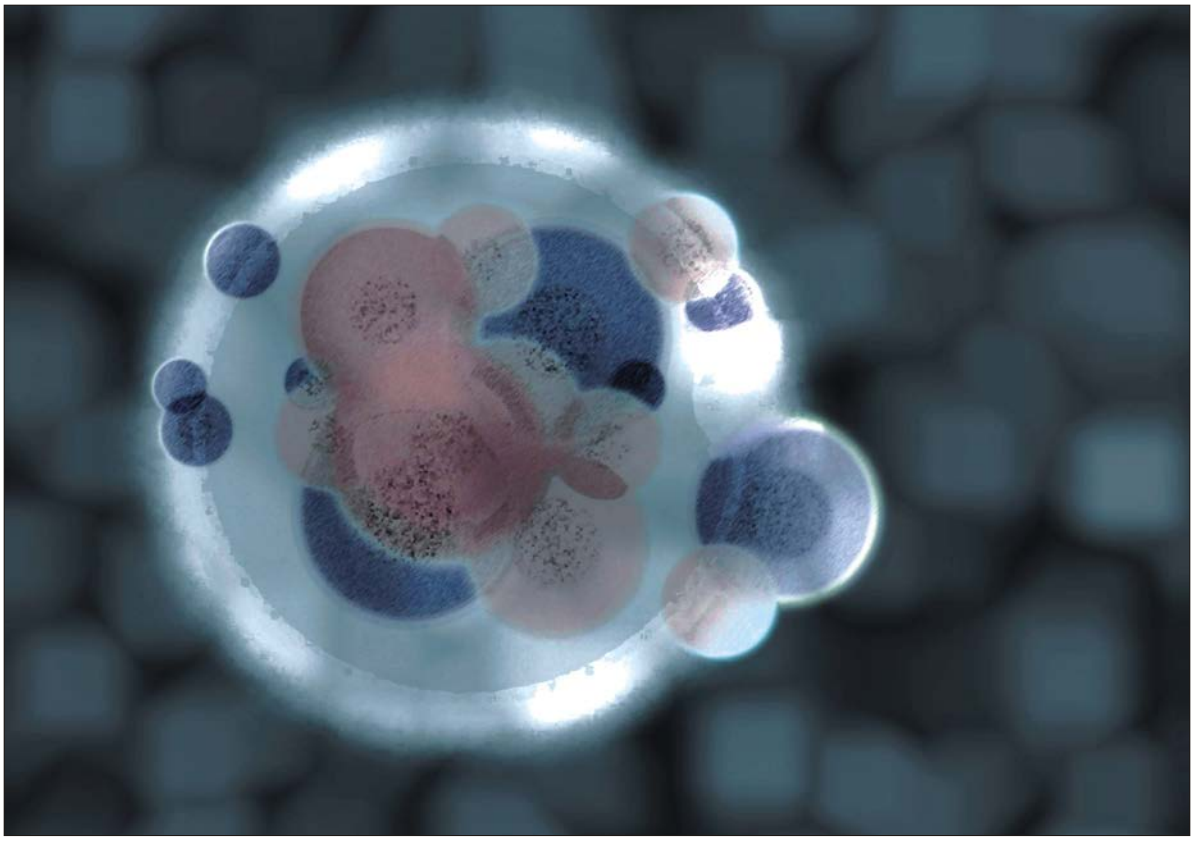

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Polluted Air Increases Obesity Risk in Young Animals

Exposure to polluted air early in life led to an accumulation of abdominal fat and insulin resistance in mice even if they ate a normal diet, according to new research.

Animals exposed to the fine-particulate air pollution had larger and more fat cells in their abdominal area and higher blood sugar levels than did animals eating the same diet but breathing clean air.

Researchers exposed the mice to the polluted air for six hours a day, five days a week for 10 weeks beginning when the animals were 3 weeks old. This time frame roughly matches the toddler years to late adolescence in humans.

The exposure levels for the animals subjected to polluted air resemble the fine-particulate pollution that can be found in urban areas in the United States.

"This is one of the first, if not the first, study to show that these fine particulates directly cause inflammation and changes in fat cells, both of which increase the risk for Type 2 diabetes," said Qinghua Sun, an Associate Professor of Environmental Health Sciences at Ohio State University and lead author of the study.

The research appears in the December issue of the journal Arteriosclerosis, Thrombosis, and Vascular Biology.

Sun and colleagues fed the mice with either a normal diet or a high-fat diet and exposed them to either filtered air or air containing at least seven times more fine particulates than the ambient air in Columbus, Ohio. On average, the ambient air contained 15.8 micrograms of fine particles per cubic meter, compared to 111 micrograms per cubic meter in the concentrated air to which the mice were exposed.

According to the U.S. Environmental Protection Agency, roughly one out of every three people in the United States is at a higher risk of experiencing health effects related to the presence of polluted air. Because of their tiny size -- 2.5 micrometers or smaller in diameter, or about 1/30th of the average width of a human hair -- these particles could reach deep areas of the lungs and other organs in the body.

For this study, researchers obtained baseline measures of the mice for their weight, blood sugar and body fat at the start of the experiment. After exposing the animals to polluted or filtered air for 10 weeks, researchers analyzed the mice for a number of risk factors associated with obesity and insulin resistance, the hallmark of Type 2 diabetes.

As expected, mice on the high-fat diet gained much more weight than those on the normal diet. But mice exposed to polluted air and eating the normal diet had more significant elevations in glucose -- sugar in their blood -- than did normal-diet mice that breathed clean air. They also showed more signs of insulin resistance based on an index that measures both sugar and insulin in the blood at the same time.

Insulin resistance results when the presence of insulin does not initiate the transfer of glucose from the blood into the tissues, where it is used for energy.

Mice exposed to pollution -- regardless of which diet they ate --also had higher blood levels of tumor necrosis factor-alpha, a protein involved in systemic inflammation, than did mice breathing clean air.

In addition, both abdominal and subcutaneous (under the skin) types of fat were increased with exposure to pollution in mice, even in animals that ate the normal diet. Mice eating a high-fat diet also had more fat, but their exposure to polluted air did not exacerbate those effects.

"These findings suggest that fine particulate pollution exposure alone, in the presence of a normal diet, may lead to an increase in fat cell size and number, and also have a proinflammatory effect," said Sanjay Rajagopalan, Senior Author of the study and the John W. Wolfe Professor of Cardiovascular Medicine at Ohio State.

Fat cell size and quantity is important in many diseases because the tissue made up of fat cells begins to secrete molecules that send out complex signals. This process can

lead to inflammation and, in turn, to insulin resistance or diabetes, as well as other disease conditions. Abdominal, or visceral, fat in particular is closely associated with the development of cardiovascular disease.

The scientists do not yet know whether these effects would be sustained over adult life if air quality circumstances were changed, or if they are otherwise reversible.

"We really wanted to see how this air pollution affects obesity with this early life exposure," Sun said. "In a real-world scenario, it would be very difficult to escape from the pervasive influence of dirty air, an influence that begins very early on in life."

Â To explore the physiological mechanism behind the pollution's effects on fat cells and inflammation, the researchers tested the same exposure levels in mice that had been genetically modified so they don't carry a gene called p47phox. This gene is a subunit of an enzyme linked to free radicals that lead to the accumulation of inflammatory cells in artery walls and plaque, known as "atherosclerosis".

"Mice without this gene that were exposed to pollution did not show most of the effects of that exposure that normal mice showed", Sun said.

"When you knock out p47phox, it pretty much alleviates the effects of air pollution," he said. "What this gives us is a potential for future therapeutic options that might target this gene."

More research would be required to further define this mechanism, he noted.

These same researchers do plan to continue studying the effects of fine particulate pollution on health, and have designed a study in humans that will take place in Beijing, China. The project, led by Rajagopalan, will test the effects of air pollution on metabolic syndrome and insulin resistance in patients. Participants will wear personal monitors to gauge their exposure to pollution.

This research is supported by the National Institutes of Health and the Diabetes Action Research and Education Foundation.

Additional Co-authors of the paper are Xiaohua Xu, Zubin Yavar and Matt Verdin of the Division of Environmental Health Sciences in Ohio State's College of Public Health; Zhekang Ying, Georgeta Mihai, Thomas Kampfrath and Aixia Wang of Ohio State's Davis Heart and Lung Research Institute; and Mianhua Zhong, Morton Lippmann and Lung-Chi Chen of New York University School of Medicine.