Ultrafine particles in air pollution may heighten allergic inflammation in asthma

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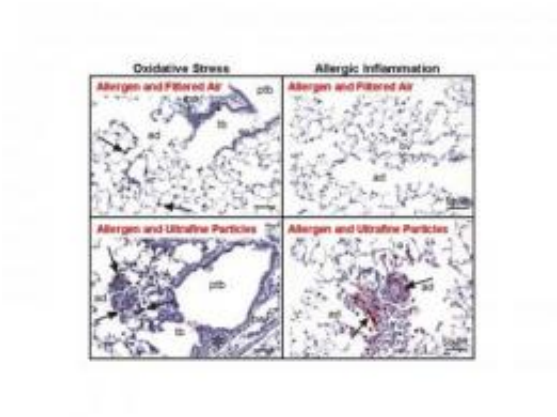

Exposure to ultrafine particles generated significantly stronger oxidative stress (lower left panel) and allergic inflammation (lower right panel) deep in the lung. Credit: UCLA

A new academic study led by UCLA scientists has found that even brief exposure to ultrafine pollution particles near a Los Angeles freeway is potent enough to boost the allergic inflammation that exacerbates asthma.

Published online in the *American Journal of Physiology-Lung Cellular and Molecular Physiology* in June, the study shows that the tiniest air pollutant particles — those measuring less than 180 nanometers, or about one-thousandth the width of a human hair — incited inflammation deep in the lungs. The researchers used a "real-time" testing method in an

animal model to isolate the effects of vehicular emission particles on the immune response in the lung.

Since these ultrafine particles are primarily derived from vehicular emissions and are found in highest concentrations on freeways, the results have particular significance for the study of the impact of traffic-related emissions on asthma flares in urban areas.

The findings also point to the importance of understanding the role air-pollution particles play in asthma flares in order to develop new approaches for asthma therapy.

"The immune processes involved in asthma, and current treatments, are traditionally thought to be dominated by a specific initial immune response, but our study shows that ultrafine pollution particles may play an important role in triggering additional pathways of inflammation that heighten the disease," said the study's principal investigator, Dr. Andre E. Nel, professor of medicine and chief of nanomedicine at the David Geffen School of Medicine at UCLA.

Pollution particles emitted by vehicles and other combustion sources are coated with a layer of organic chemicals that can be released into the lungs. These chemicals generate free oxygen radicals, which excite the immune system in the lung through a cell- and tissue-

damaging process known as oxidation. Oxidation contributes to allergic inflammation in the lungs of people with asthma.

Although other studies have shown that larger air-pollution particles can cause an oxidative response in asthma, this is the first study to show that real-time breathing of collected ultrafine pollutant particles triggers the same reaction and may even be more damaging, due to the particles' tiny size, the researchers noted.

Because of their size and large surface area, ultrafine particles have the capacity to carry and deposit a rich load of active organic chemicals deep in the lung. The chemicals coming off the particles in the small airways in the lung promote oxidative stress at those sites.

In the study, researchers initially gave mice a surrogate allergen, similar to exposing humans to an allergen such as pollen. After further sensitization, half the mice received ultrafine pollutants, taken in real time near a freeway in downtown Los Angeles, while the other half breathed filtered air.

The study utilized sophisticated exposure technologies developed by Dr. Costas Sioutas, the Fred Champion Professor of Civil and Environmental Engineering at the University of Southern California and co-director of the Southern California Particle Center. The multicampus team also included researchers from Michigan State University and the University of California, Irvine. The research at the Southern California Particle Center and the UCLA Asthma and Allergic Disease Center was funded by the U.S. Environmental Protection Agency and the National Institutes of Health.

Researchers found that exposure to air containing ultrafine particles for a few hours a day over five days significantly enhanced allergic airway inflammation, which correlated to the changes found in the immune system and genes expressed. Scientists discovered that the most profound effects of the allergic inflammation were observed deep in the lung.

"We found that even small exposure amounts to the ultrafine particles could boost the pro-inflammatory effects," said first author Ning Li, an assistant researcher in the UCLA Division of Nanomedicine.

The level of ultrafine particle exposure in the study was two to five times

higher than levels commuters are subject to while traveling in their vehicles on Los Angeles freeways.

Researchers noted that the development of asthma may be more complicated than originally thought, with mounting evidence pointing to the involvement of additional pathways of immune activity associated with the effects of oxidative stress.

"A number of new therapies are now targeting the role of oxidative stress in asthma exacerbation," Nel said. "One possible strategy may be the use of antioxidants that may interfere with development of oxidative stress."

In addition to new considerations for asthma treatment, the study findings may also help epidemiologists further establish the link between surges of pollutants near freeways and asthma flares and to pinpoint the amount of ultrafine particle concentrations involved.

The next stage of research will help identify the chemical components responsible for boosting the effect of particulate pollutants on the allergic inflammation found in asthma and will explore the immunological mechanisms behind it at the molecular level.

Asthma, which affects 15 to 20 million people in the United States, is a chronic inflammatory disease of the small airways in the lung and can trigger acute episodes of airway tightening and wheezing.

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