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Ozone shuts down early immune response in lungs and body

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As policy makers debate what levels of ozone in the air are safe for humans to breathe, studies in mice are revealing that the inhaled pollutant impairs the body's first line of defense, making it more susceptible to subsequent foreign invaders, such as bacteria.

While it has long been known that exposure to ozone, a major component of urban air pollution, is associated with increased cardiovascular and pulmonary hospitalizations and deaths, the actual mechanisms involved remain unclear. New studies by Duke University Medical Center pulmonary researchers on the effects of ozone on the innate immune system, the body's "tripwire" for foreign invaders, may provide part of the answer.

The Duke-led team found that ozone exposure in mice at levels approximating unhealthy levels for humans appears to enhance lung injury in response to bacterial toxins, but more importantly, it also appears to enhance programmed cell death in critical innate immune system cells that gobble up foreign invaders, keeping the airways clear.

"Small amounts of inhaled foreign material can be relatively harmless, since they stimulate an appropriate innate immune response that protects the lungs," said John Hollingsworth, M.D., pulmonologist and lead author of study whose results appear Oct. 1 in the *Journal of Immunology*. "However, it appears that ozone causes the innate immune system to overreact, killing key immune system cells, and possibly making the lung more susceptible to subsequent invaders, such as

bacteria."

The innate immune system is the most primitive aspect of the body's defenses. Its cells react indiscriminately to any invader. One of the key cells in the innate immune system is known as a macrophage, Greek for "big eater."

For their experiments, the researchers had mice breathe either room air or air with levels of ozone meant to mirror what an exercising human would experience on a high, or unhealthy, ozone level day. After exposing all mice to the active portion of E. coli bacteria in aerosol form, the researchers studied how the innate immune system responded.

"In the mice exposed to ozone, the airways of the lungs were hyperactive and we found higher concentrations of inflammatory cells," Hollingsworth said. "But more significantly, ozone pre-exposure reduced the number of macrophages in the lung after secondary exposure to inhaled bacterial endotoxin. Exposure to ozone in this context had stimulated them to undergo programmed cell death, or apoptosis."

The researchers also found that the effect of the inhaled ozone was not limited to just the lungs. Mice exposed to ozone were also found to have lower levels of immune system cells circulating in the blood.

The Duke team plans further studies on the mechanisms behind ozone's ability to induce cell death in macrophages in the lungs. They will also focus on the pollutant's ability to interfere with system-wide immune responses.

The Environmental Protection Agency is in the final phases of reviewing and possibly updating the standards for allowable levels of ozone in the air. The current standard says that any amount greater than 85 parts per billion can be unhealthy for those at risk. Many medical groups,

including the American Thoracic Society, recommend setting a stricter standard of 60 parts per billion, citing studies showing ozone's adverse effects on health, especially in children and those with compromised health.

Source: Duke University