Secondhand smoke may provoke inflammatory response in lungs

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Second-hand smoke is associated with a number of diseases and conditions, including cancer, heart disease, and emphysema. It is an irritant to lung tissue and blood vessels, but the processes through which the body reacts to second-hand smoke comprise a mystery scientists are only beginning to unravel. Researchers at the University of Colorado-Denver are currently studying how second-hand smoke affects the lungs of rats, and so far it appears that second-hand smoke triggers a complex inflammatory response.

Adelheid Kratzer, an investigator in the Department of Medicine's Division of Pulmonary and Critical Care under principal investigator Laima Taraseviciene-Stewart, will present the team's research at the 2010 American Physiological Society (APS) conference, Inflammation, Immunity, and Cardiovascular Disease, in Westminster Colorado, August 25-28.

To determine how lung tissue may respond to second-hand smoke, the team exposed male Sprague Dawley rats to second-hand smoke in a special chamber 5 times per week for two months or four months. The exposure was a mixture of 89% sidestream smoke, which comes from the end of a lit cigarette and is exposed to the whole body, and 11% mainstream smoke, which is smoke directly inhaled by the rats. The rats were exposed for two three-hour shifts twice a day, separated by a two-hour break.

This ratio was chosen because of its similarity to the human experience

with second-hand smoke, said Dr. Kratzer. "This is much like what a human would be exposed to at a bar or casino."

Other rats were assigned to the control group and were exposed only to regular room air. At the end of each group's exposure, the rats were euthanized and the researchers extracted and studied the rats' lung tissue.

Two months of exposure to second-hand smoke were enough to cause significant changes in the rats' lung tissue, and the results were even more profound in rats exposed for four months. First, the researchers observed enlargement in the alveolar air space of the rats' lungs. That is, the space in the lungs' alveoli, the tiny sacs where oxygen-carbon dioxide exchange takes place during respiration, increased. This suggests that the alveolar structure had begun to break down, much as it does in early emphysema.

The researchers also noted increased numbers of white blood cells called macrophages in the alveolar space of the rats exposed to second-hand smoke, indicating that the rats' bodies had mounted an immune response. What's more, the macrophages were distorted, said Dr. Kratzer. "They had an odd shape, as if they had engulfed particles, which might impair their function."

There were also increased levels of interleukin-18, a cytokine produced by macrophages and associated with strong inflammatory reactions and tissue destruction.

Finally, the researchers observed that second-hand smoke appeared to inhibit the growth and proliferation of endothelial cells in the small blood vessels of the rats' lungs, an effect that is underlined by in vitro studies. Endothelial cells line the inside of blood vessel walls and serve as a barrier between the inner space of the blood vessel and surrounding tissue. They also control the transit of white blood cells into and out of

the bloodstream. Decreased endothelial cells render the blood vessel wall less elastic and more permeable, which can lead to chronic inflammation as seen in chronic obstructive pulmonary diseases like emphysema and chronic bronchitis.

The team noted that treatment with alpha-1-antitrypsin, a protein made in the liver that is normally present in the blood and protects the lungs and other tissue from the damaging effects of tissue-degrading enzymes produced by inflammatory cells. In humans, a deficiency of this protein causes lung disease.

The team's research may have broad implications for the treatment of damage caused by second-hand smoke in humans, said Dr. Kratzer. "We found different enzyme markers distinctively regulated upon smoke exposure," she said. "Regulation of these markers may indicate a way we could try to try to protect the tissue from destruction in addition to alpha-1-antitrypsin activation."

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