Chronic drinking and exposure to particulate matter dramatically decreases lung function

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Alveolar macrophage (AM) function plays a critical role in protecting the lungs from particulate matter inhalation by removing particulates from the airway and secreting elements that facilitate airway repair. Chronic drinking causes persistent oxidative stress in the lungs, leading to impaired AM function as well as immune responses. A rodent study has found that chronic drinking, when coupled with particulate matter (PM) exposure, dramatically increases lung dysfunction compared to alcohol intake or PM exposure alone.

Results will be published in the November 2013 issue of *Alcoholism: Clinical & Experimental Research* and are currently available at Early View.

"Macrophages are derived from monocytes, a subset of the white blood cells present in the body," explained Stephania A. Cormier, associate professor of pediatrics – currently at the University of Tennessee Health Science Center – as well as corresponding author for the study. "Under normal conditions, monocytes travel into the tissues of the body and mature into macrophages. In the tissues, they perform activities necessary to maintain normal functions and, along with other tissue resident immune cells, provide an initial layer of protection against invading pathogens. AMs, present throughout the large and small airways of the lungs, secrete factors that assist normal airway function while also serving a janitorial role by engulfing and removing inhaled debris and dead cells from the airways."

"The lung has 100s of millions of macrophages," added George Leikauf, professor of environmental and occupational Health at the University of Pittsburgh. "The term derives from macro = big + phage = cell that eats. Their main job is to 'eat' or phagocytize bacteria and particles that land on the alveolar surface. Once bacteria are engulfed, the macrophages kill the bacteria. When particles are engulfed that cannot be digested, macrophages retain the particles and then move up the airways to clear the particle from the lung. In humans, the alveolar surface is about the size of a tennis core, so these cells have a massive responsibility. Normally, macrophage are very efficient and kill all the bacteria, thus the alveolar region is sterile. However, when compromised the macrophage cannot keep up with this duty, and bacteria grow. This can result in a lower respiratory tract infection such as pneumonia, which is the third leading cause of death in the US."

"While research has yet to define the precise mechanisms of how alcohol consumption increases the levels of reactive oxygen species in the lungs, we do know that alcohol alters numerous processes on the cellular level," said Cormier. "Specifically, a portion of alcohol ingested is metabolized in the lungs by a detoxification pathway which is less efficient than the primary metabolism pathway used in the liver. This less efficient pathway produces reactive products which must be further metabolized within the cell, using up antioxidants available within the cell. Alcohol also reduces the ability of the cells to replenish these antioxidants. As a result, reactive oxygen species increase within the cell, where they react with cellular components, altering or completely destroying their function. This cycle continues with daily alcohol consumption, directly increasing oxidative stress while also impairing the ability of our cells to maintain and increase antioxidant defenses."

Cormier and her colleagues fed age- and gender-matched C57BL6 mice a liquid diet that contained either alcohol or an iso-caloric substitution for eight weeks. During the final two weeks, mice from both groups

were exposed to combustion-derived PM. Study authors then assessed AM number, maturation, and polarization status; in addition, both invasive and noninvasive methods were used to assess pulmonary function and correlate it with histomorphological assessments of airway structure and matrix deposition.

"We already knew that PM derived from automotive, industrial, hazardous waste processes, and other combustion processes aggravates existing lung disease and can predispose children and other susceptible individuals to pulmonary diseases such as asthma," said Cormier. "Here we found that chronic drinking, when coupled with PM exposure, dramatically decreases antioxidant defenses in the lungs compared to alcohol intake or PM exposure alone. This was accompanied by a decrease in the number of AMs present in the lungs immediately following PM exposure. Furthermore, the AMs that were present in the airways after exposure to both alcohol and PM [had] dramatically altered function. Collectively, chronic drinking amplifies the effects of PM exposure and accelerates declines in lung function due to PM exposure."

"This study is unique in that – by examining the combined insults of excessive alcohol and inhaled particles together – the study comes closer to the human experience in that we are often exposed to more than one adverse life style or environmental risk factor," added Leikauf. "Results suggest these two events can initiate damage to lung tissue and decrease the mice's capacity to breathe. While the effects are small and the study was only conducted over a short period of time, these risk factors can persist in humans over a lifetime. As with any animal study, caution needs to be paid to species' differences in susceptibility, but this study supports additional evaluation of the combined effects of such risk factors in a large human population."

"The relationships between alcoholism and PM exposure are particularly concerning given an estimated 18 million people in the US with alcohol

use disorders and the high percentage of individuals who heavily consume alcohol and smoke cigarettes, which is a source of combustion-derived PM," added Cormier. "Therefore, our model of chronic alcohol intake and exposure to PM mimics a very real-world scenario."

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