

Infection Blocks Response

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DENVER — An infection that often goes undetected can block the lung's natural protective response against tobacco smoke, according to researchers at National Jewish Health. The findings, recently published online and scheduled to appear in the October issue of *Infection and Immunity*, suggest one mechanism that may cause smokers to develop chronic obstructive pulmonary disease.

“Although smoking is the overwhelming cause of chronic obstructive pulmonary disease (COPD), only 20 percent of smokers develop the disease,” said Brian Day, senior author on the study and Professor of Medicine at National Jewish Health. “Our findings suggest that *Mycoplasma pneumoniae* (*Mp*) infection may be one of the co-factors that lead to COPD and other diseases among smokers.”

Tobacco smoke contains more than 4,700 chemicals, which generate approximately 100 trillion reactive molecules per puff. Those molecules, known as reactive species, can damage lung tissue by chemically reacting with DNA, cell membranes and other molecules in the lung.

It has long been known that the lungs mount a strong protective response against tobacco smoke, which the National Jewish researchers confirmed in their studies in mice and cell cultures. They found that mice exposed to tobacco smoke for 16 weeks doubled the amount of the antioxidant glutathione in the fluid bathing the airways. The antioxidant reacts with the reactive species in tobacco smoke, thus preventing damaging reactions with lung tissue.

“This natural protective response actually allows people to smoke,” said Day. “Without it, all smokers would suffer significantly more lung damage.”

Previous work in Dr. Day's lab had suggested that lung infections might affect the lung's protective response. And work in Dr. Richard Martin's lab at National Jewish has implicated the organism *Mycoplasma pneumoniae* (*Mp*) in worsening asthma. *Mp* is a common lung pathogen and the most common cause of pneumonia, but can be difficult to detect because it is challenging to grow in culture. Recent tests to detect *Mp* DNA in the lungs have indicated that it may be more prevalent than generally recognized and can exist as a low-level chronic infection.

When Dr. Day and his colleagues infected mice with *Mp* it had a mild effect, slightly lowering glutathione levels in the lungs of mice breathing fresh air. When mice were exposed to tobacco smoke then infected with *Mp*, glutathione levels dropped even lower.

“The *Mycoplasma* infection completely blocked the protective response mice normally mount against tobacco smoke, reducing antioxidant levels well below even those of mice breathing fresh air,” said Dr. Day.

After glutathione reacts and neutralizes reactive species in the lungs, it becomes oxidized. Under normal conditions mice and humans produce an enzyme, called glutathione reductase (GR), which recycles the oxidized glutathione into its protective, reduced state. The researchers found that mice exposed to tobacco smoke and *Mp* had much higher levels of oxidized glutathione along with the low levels of reduced glutathione. The researchers also found that the *Mp* infection significantly lowered levels of GR in mice lungs.

“The *Mycoplasma* infection blocked the lungs' protective response to tobacco smoke by lowering levels of the enzyme that normally recycles oxidized glutathione back into its protective, reduced form,” said Dr. Day. “This resulted in severe oxidative stress and increased tissue damage as measured by oxidized DNA.”

“These higher levels of oxidative stress and damage are likely to predispose smokers with *Mycoplasma* infections to lung disease, such as COPD or cancer.”

National Jewish Health is the leading respiratory hospital in the nation. Founded 120 years ago as a nonprofit hospital, National Jewish Health today is the only facility in the world dedicated exclusively to groundbreaking medical research and treatment of patients with respiratory, cardiac, immune and related disorders. Patients and families come to National Jewish Health from around the world to receive cutting-edge, comprehensive, coordinated care. To learn more, visit the media resources page.

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