

Obesity combined with exposure to cigarette smoke may pose new health concerns

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Millions of people who are obese and smoke tobacco may face additional health problems—including their responses to common prescription medicines—that extend beyond the well-known links with cancer, heart attacks and stroke, according to a report presented here today.

Scientists told an audience at the 246th National Meeting & Exposition of the American Chemical Society (ACS), the world's largest scientific society, that those health threats may include "passive" or "second-hand" smoking. It occurs when non-smokers inhale smoke from cigarettes smoldering nearby. The ACS meeting, which continues through Thursday, includes almost 7,000 reports on new advances in science and other topics.

"Our research shows that smoking and obesity together may pose a triple health threat in addition to the increased risks for heart disease, cancer and diabetes," said Aaron Wright, Ph.D., who reported on the study.

"That dangerous combination impacts key mechanisms by which both the lung and liver perform metabolism. For example, the body's ability to metabolize prescription drugs may be altered in ways that could make standard dosages too high or too low to be effective in obese people who are exposed to tobacco smoke.

"Tobacco smoke and obesity also intensifies the cancer-causing potential of [cigarette smoke](#). We were surprised to find that in some instances, the substances in second-hand smoke seem to have a more dramatic effect

than just smoking," he said.

Wright described experiments analyzing the activity of a key family of enzymes in liver and lung tissues obtained from lean and obese mice exposed directly to cigarette smoke and second-hand smoke. These cytochrome P450 enzymes (also known as "P450s") metabolize, or break down, about 75 percent of all prescription and non-prescription drugs, and other ingested substances. The P450 enzyme system ensures that insulin, beta-blockers, oral contraceptives, pain-relievers, tranquilizers and other medications do their work and then disappear from the body. P450s also metabolize fats.

Scientists have known for years that cigarette smoke can make some P450 enzymes more active. As a result, smokers may wind up with levels of medication in their blood that are too low to treat a disease. Though they haven't studied many obese individuals, researchers know that some alterations to the activity of P450 enzymes occur with excess body weight.

Wright and colleagues, who are with the Pacific Northwest National Laboratory in Richland, Wash., decided to take a first step toward determining the combined effects of both cigarette smoke and obesity. With obesity a problem for about 72 million people in the United States alone, and 44 million people still smoking cigarettes, they knew that considerable overlap occurs, with millions of people both obese and smokers. They studied how P450 enzymes work in liver and lung tissues from groups of mice that were obese or normal weight, and exposed to cigarette smoke, second-hand smoke, or not exposed to cigarette smoke.

"Exposure to cigarette smoke increased the activity of some of the P450 enzymes, and adding obesity had little or no change on that effect," Wright said. "But for other enzymes, which usually are far more active when exposed to cigarette smoke, the addition of obesity had a dramatic,

opposite effect. The enzymes were 100 times less active."

One potential consequence of these combined effects is an increased risk of developing lung cancer, Wright said. He explained that substances in cigarette smoke become carcinogenic when the P450s break them down. Obesity alters the lung P450s, potentially adding to the [cancer](#)-causing effects of the smoke.

A look at second-hand smoke revealed more surprises. Second-hand smoke had a more pronounced effect on the activity of some enzymes than active smoking.

Wright said it will take additional research to establish the exact health implications for the millions of people who smoke and are obese. But the findings, he added, are another reason why people should maintain a normal body weight and avoid cigarette smoke. And they may serve as an alert to pharmaceutical companies to consider both cigarette smoke exposure and obesity in drug research.

More information: Abstract:

Activity-based protein profiling reveals systemic effects of smoking and obesity on cytochrome P450 function

Obesity and tobacco smoking have long been implicated in the induction and inhibition of phase I metabolism by cytochrome P450 (P450) enzymes in the lung and liver. We hypothesized that mainstream and sidestream smoking would have broad effects upon P450 function, and when coupled to obesity the effects would be pronounced. To test this we employed a multiplexed activity-based protein profiling approach to isolated lung and liver microsomes from lean and obese mice that were mainstream, sidestream, or non-smokers. Proteomic measurements of probe-labeled proteins identified organ-dependent and broader systemic

effects on the function of nearly 30 P450s, with significant induction and inhibition of P450 function in lean and obese mice. These studies reveal that the combination of smoking and obesity is highly detrimental to phase I metabolic function, contributes to the known intolerance to and rapid clearance of therapeutic drugs, and increases the carcinogenic potential of tobacco smoke constituents.

Provided by American Chemical Society

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