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How much smoking is safe? The answer appears to be none

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Smokers often wonder if smoking less might be safer for their health. The answer appears to be no. Occasional smoking, and even second-hand smoke, create biological changes that may increase the risks of lung disease and cancer, according to a new study.

Even at the lowest detectable levels of nicotine in urine, the genes most sensitive to tobacco smoke in cells lining the lungs' airways begin to function differently, reports a study authored by Cornell and NewYork-Presbyterian Hospital/Weill Cornell Medical Center (NYPH/WCMC) researchers and published Aug. 20 in the American Journal of Respiratory and Critical Care Medicine.

This is the first study to show that even minimal exposure to tobacco smoke triggers signs of detectable smoking stress in the genomewide gene expression profile of the lung. The technique developed for the study, which analyzed some 372 genes known to be sensitive to smoking, could potentially be used to detect the onset of a number of other nonsmoking related diseases.

To diagnose the start of lung disease, "you'd have to follow someone who smokes for many years, but what we have here is a signal that shows up at very low levels," said Larsson Omberg, a postdoctoral researcher in biological statistics and computational biology (BSCB) and one of the paper's lead authors.

As a technique applicable to nonsmoking related diseases, "it's a

foundation that we can build on," added co-author Jason Mezey, an assistant professor in BSCB, whose lab directed the statistical analysis.

Dr. Ronald Crystal, senior author of the study and chief of pulmonary and critical care medicine at NYPH/WCMC, analyzed the urine (for nicotine and cotinine, the chemical into which the liver breaks down nicotine) and cells from the small airways of the lung of 121 individuals. Urine nicotine and cotinine levels were used to categorize volunteers as nonsmokers or occasional or heavy smokers.

Omberg, Mezey and colleagues drew upon various methods for analyzing genes quantified by microarray analysis. By combining methods, they created a new process that allowed them to see the effects of smoking on single genes as well as the entire genome at very low levels of exposure.

The researchers found that in the volunteers with "low exposure" to smoking, more than one-third of the 372 genes sensitive to smoking were triggered. (Some genes have lower expression and some genes have higher expression when exposed to tobacco smoke). This smoke stress was observed even when urine nicotine was below detectable levels, and when urine cotinine was just barely above detectable levels.

Also, the study found, heavy smokers triggered more of these genes and the expression of individual genes increased accordingly.

"The model allows us to predict, based on nicotine and cotinine levels, how much a gene may be expressing," said Omberg. The method also allowed them to analyze all genes across the genome as one function. "Using genomewide data, one can extract more subtle patterns of the effects of low levels of exposure," added Mezey.