Gender May Render Women at Risk for Lung Cancer

Skyrocketing lung cancer deaths in women since 1950 may be due to more than increased smoking. A new study suggests that women may be more susceptible to DNA-damaging carcinogens than men.

In a retrospective analysis of lung cancer cases between 1981 and 1994, researchers at the American Health Foundation in New York found that women's susceptibility to lung cancer may go beyond their exposure to smoking — the leading cause of this type of cancer. Results of the study appear in this issue of the Journal (see page 183).

"I believe that it is likely — conceptually — that there is an endogenous factor that increases a woman's risk," said Ernst L. Wynder, M.D., a principal investigator of the study and president of the New York foundation. Wynder and his co-investigator, Edith A. Zang, Ph.D., offer several possible explanations for the gender gap: hormonal factors, particularly estrogen, and differences in how women process and detoxify carcinogens, including those in tobacco smoke.

"The main point here is that women begin smoking later than men, they smoke fewer and lighter [tar] cigarettes than men ... and yet they have a higher risk of developing lung cancer," Wynder said. "Our paper is saying that we cannot afford to ignore this epidemic of lung cancer in women."

Since 1987, lung cancer has been the leading cause of cancer death in women, surpassing breast cancer. And while lung cancer incidence has leveled off among men, it continues to rise steadily among women. This increase in incidence, Wynder and Zang contend, "exceeds that expected from a slower decline of smoking among women."

All Types of Lung Cancer

The researchers looked at 3,959 patients: 1,889 lung cancer cases and 2,070 patients admitted to the hospital for diseases unrelated to smoking, such as arthritis, as controls. The researchers found a statistically significant gender difference in lung cancer risk between women and men for all three major histologic types of lung cancer — adenocarcinoma, small-cell oat cell carcinoma, and squamous/epidermoid cancer — given the same levels of long-term exposure to cigarettes.

Overall, women had an approximately 1.5-fold-higher estimated relative risk than men for developing lung cancer, with that risk most pronounced for adenocarcinomas and small-cell lung cancers. However, the results also suggest, the researchers said, that this increased risk "may apply to nonsmokers as well, since the proportion of never-smoking lung cancer patients was more than twice as high in women as in men."

In future studies, Wynder said, one area of emphasis will be the potential association between estrogen replacement therapy and adenocarcinomas of the lung. In the current study, he noted, women 55 years old or older with this type of lung cancer were nearly twice as likely never to have smoked than younger women with adenocarcinomas — a finding that may be explained by estrogens. Cells with estrogen receptors line not only the breast, but the lungs as well, Wynder pointed out.

Meanwhile, researchers at the American Health Foundation will also begin looking at differences in lung cancer risk among African-Americans.

"Blacks smoke less, but have higher rates of lung cancer than whites," said Zang.

Commenting on the science supporting gender differences in lung cancer risk in general, Neil Caporaso, M.D., a researcher in the National Cancer Institute's Division of Epidemiology and Genetics said that so far "it's not very solid." But while older data suggest men are at greater risk than women for lung cancer, more recent studies suggest that these differences don't persist, he added, and "women may be more vulnerable to this disease after adjusting for smoking."

— Susan Jenks

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