Dear Friends,

Lung cancer causes more deaths in men and women than any other cancer, yet other cancers continue to receive more attention. It is also the least-funded cancer, in terms of research dollars per death, of all the cancers. It is estimated that 90% of lung cancer deaths in men and 80% in women can be attributed to smoking. Despite the growing knowledge that smoking causes lung cancer, most of the new smokers today are teenage girls!

While exposure to other carcinogens can also cause lung cancer, their combined effect is small compared to smoking, the most preventable cause of cancer in the United States. This edition of the Institute for Women’s Health Research e-newsletter focuses on sex and gender differences related to smoking and its impact on health.

The Institute Staff

Women and Lung Cancer

Incidence and Mortality

According to the American Cancer Society’s most recent estimates for lung cancer in the US, in 2009 there will be:

- 159,390 deaths (88,900 among men and 70,490 among women), accounting for 28% of all cancer deaths.
- More people who die of lung cancer than of colon, breast, and prostate cancers combined.

While the incidence of lung cancer has declined in men, it increased six-fold in women over the last 30 years. During this same time period, the death rate from lung cancer has declined in men, while
30 years. During this same time period, the death rate from lung cancer has declined in men, while the death rate from lung cancer in women increased through 2003, and only recently is leveling off. Smoking prevalence is still lower among women than men (18% vs 23%) but smoking rates in men are falling at a higher rate than women. While this article focuses on lung cancer, it is worth noting that, according to the World Health Organization, cigarette smoking causes other illnesses besides cancer and together they kill more than 173,000 women in the U.S. each year. Smoking also increases the risk for other types of cancer, as well as heart disease, asthma, infertility, and the future health of unborn children.

About 2 out of 3 people diagnosed with lung cancer are older than 65; fewer than 3% of all cases are found in people younger than 45. The average age at the time of diagnosis is about 71. Overall, the chance that a man will develop lung cancer in his lifetime is about 1 in 13; for a woman, the risk is about 1 in 16. These numbers include both smokers and non-smokers as non-smokers who breathe in second-hand smoke are at increased risk for lung cancer.

Sex and Gender Differences in Lung Cancer and Smoking Habits

An individual's risk for developing lung cancer may be influenced by both sex and gender factors. Sex differences refer to the physical and biological characteristics that identify a person as male or female. Gender, however, is largely a social construct that associates certain behaviors, roles, expectations, and values as being male or female. Mounting research suggests that genetic, hormonal, behavioral and environmental factors are influencing the different patterns of lung cancer in women and men.

Sex factors include genetic susceptibility and hormone levels. Gender factors include age when smoking began, how deeply one inhales, type of cigarette smoked, as well as social factors that influence smoking behavior. Some of the current observations that point to sex/gender differences are:

- Lung cancer develops differently in women and men.
- Women who have never smoked appear to be at greater risk for developing lung cancer than men who have never smoked: One in 5 women and 1 in 12 men diagnosed with lung cancer today have never smoked!
- Women tend to develop lung cancer at younger ages than men.
- Women are more likely than men to be diagnosed in early stages of lung cancer.

Women generally live longer than men from lung cancer, regardless of the stage at diagnosis, type of lung cancer or treatment choices. The reasons for this disparity are unclear. Even when studies adjust for type and stage of cancer and treatment, being female persists as an independent factor to increased survival following surgery. Additional investigation is needed to understand the interaction of factors that seem to contribute to women's advantage in survival.

Lung cancer is often diagnosed 20-30 years after exposure and, historically, women began smoking in large numbers decades later than men. Today we are beginning to see the result of the increase in female smokers that began several decades ago.

Role of Hormones

Studies have found a possible connection between hormones, such as estrogen, and lung cancer development, particularly adenocarcinoma (the most common type of lung cancer in men and women of all ages). Researchers believe estrogen can directly or indirectly promote lung cancer by triggering estrogen receptors that are present on certain lung cancer cells, causing them to grow and spread.

The landmark Women's Health Initiative study found mixed results related to Hormone Replacement Therapy (HRT) and lung cancer. In postmenopausal women, combined estrogen and progesterone HRT did not increase the risk for developing lung cancer in general. However, women who took combined HRT had an increased risk of dying from certain types of lung cancer. In a more recent study just released in August 2010, researchers found that women who took estrogen only, did not have an increased incidence or death rate from lung cancer (J Natl Cancer Inst. 2010 Aug 13). These findings suggest that women who have lung cancer or who are at high risk, discuss hormone use with their physicians.
Tobacco Exposure Susceptibility
Although the link between smoking and lung cancer is indisputable, whether women and men differ biologically in their susceptibility to smoking-related lung cancer remains fiercely contested. Exposure to tobacco smoke contributes to many genetic changes and mutations in the lung. Researchers have identified 323 genes whose activity is influence by smoking, including many associated with immune response, and more than 70 cancer related genes. Women appear to have significantly more DNA damage and mutations, even if they smoke less than men. Such genetic changes may influence the development of tumors by affecting the body's capacity to break down and remove tobacco carcinogens in the lungs. Experts report that women may be less able to repair DNA damage than men, which would make them more likely to develop lung cancer.

Recent studies are focusing on a defective tumor-suppressing gene that may explain the development of lung cancer in non-smokers. Given the significant rise in lung cancer in women over the past 30 years, further research on the complex interactions of these genetic and molecular factors are warranted.

Screening
There is no widely accepted screening test for lung cancer and thus it is rarely found in its earliest, most treatable stage. Only 16% of cases are found before the disease metastasizes. X-rays and CT scans are the only available screening tools for lung cancer but there is a lot of debate regarding the benefits, risks and costs of these tools as a screening (vs. diagnostic) tool. Some critics feel that repeated exposure to CT scans may result in too much radiation. However, a first-ever study employing actuarial analyses to evaluate the effect of early detection on mortality concluded that early-stage diagnosis could significantly lower lung cancer mortality, perhaps saving as many as 70,000 lives in the US each year (Goldberg S, Mulshine J, Hagstrom D, et al. Popul Health Mag, Feb 2010). Several new diagnostic tools, including biomarkers, are in early stages of investigation.

Scientists are looking at several genetic markers including gastrin-releasing peptide receptor (GRPR) and epidermal growth factor receptor (EGFR) that may predispose some people to lung cancer. Both of these receptors have a role in cell division and growth.

Targeting Messages to Women
Tobacco advertisers recognize the importance of using sex and gender differences to target their messages, especially to women, and this may be the reason more teen girls are smoking. According to the website of the Partnership for a Tobacco Free Maine:

- Girls and women are more likely to fear weight gain than boys, and to initiate and continue smoking for weight control; women gain more weight after quitting than men.
- Women and girls tend to smoke as a buffer against negative feelings while males smoke more from habit or to enhance positive sensations.
- Low-income mothers in Western countries use smoking as a form of relaxation when taking a break from the demands of young children.
- Female addiction may be reinforced more by the sensory and social context of smoking, rather than by nicotine, suggesting that patches may be less effective in women.
- Relapse rates in women are higher, and it may take several attempts before they can succeed.

Funding and the Stigma of Smoking
The stigma attached to lung cancer may contribute to the underfunding of research on the disease. Because smoking is the primary cause, people suffering from lung cancer are thought to be responsible for their own illness, and consequently not deserving of the same unconditional sympathy of research investment as patients affected by other deadly illnesses. Even physicians who treat advanced lung cancer patients are not immune to this bias. However, it should be remembered that more complex factors than simply smoking are involved.

Sources:
Out of the Shadows: Women and Lung Cancer (pdf), Women's Health Policy and Advocacy Program, Boston
The Healthy Woman, US DHHS.
HHS HealthBeat (August 19, 2010)
Upcoming Events

September 18, 2010
Third Annual Community Baby Shower: Birth, Baby and Beyond, Prentice Women’s Hospital

September 21, 2010
Institute for Women’s Health Research Monthly Forum
Untangling the Web of Women, Smoking and Weight with guest speaker, Bonnie Spring, M.D.

September 27, 2010
Office of Research on Women’s Health 20th Anniversary Celebration

October 28 - 31, 2010
12th Annual Lynn Sage Breast Cancer Symposium

Health Tip:

If you are having trouble quitting smoking, remind yourself that it does not take very long for your body to respond favorably to smoking cessation.

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<thead>
<tr>
<th>Time After Quitting</th>
<th>Benefit</th>
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<tr>
<td>20 minutes</td>
<td>Your heart rate drops.</td>
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<tr>
<td>12 hours</td>
<td>Carbon dioxide in your blood drops to normal.</td>
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<tr>
<td>2 weeks - 3 months</td>
<td>Your heart attack risk begins to drop; your lungs work better.</td>
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<tr>
<td>1 month - 9 months</td>
<td>Coughing, sinus congestion, fatigue and shortness of breath decrease; lungs function better, lowering risk of lung infections.</td>
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<tr>
<td>1 year</td>
<td>Your risk of heart disease is half that of a smoker.</td>
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<tr>
<td>5 years</td>
<td>Your risk of having a stroke is the same as a nonsmoker.</td>
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<tr>
<td>10 years</td>
<td>Your risk of dying of lung cancer is half that of a smoker’s; your risk of mouth, throat, esophageal, bladder, kidney and pancreatic cancer decreases.</td>
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<tr>
<td>15 years</td>
<td>Heart disease risk is now the same as someone who does not smoke.</td>
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Join the Illinois Women’s Health Registry

On August 30, 2010 the Illinois Women’s Health Registry reached its September 1 goal of 5,000 participants. Special thanks to Illinois BlueCross-BlueShield for promoting the registry in their Lifetimes newsletter. Our next challenge is to reach 7,500 by the end of the year! If you have not joined yet, please do, and encourage your family and friends, to help us advance women's health research!

Forward email