

Lung Cancer Environmental Risk Factors

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Environmental Risk Factors for Lung Cancer

At about the time that the association between tobacco smoking and lung cancer was confirmed, evidence also was obtained regarding the causal relationship between asbestos and lung cancer. In addition, other risk factors—such as radon, occupational chemicals, and environmental tobacco smoke (ETS)—were identified as possible lung carcinogens.

The association between smoking and lung cancer cannot be evaluated properly without considering the influence of many variables. These variables include environmental agents, as well as unmodifiable risk factors, such as age, sex, race, and genetics.

Alcohol

People who smoke may tend to drink more alcoholic beverages and coffee and consume more non-narcotic pain relievers than nonsmokers. Several studies have reported a relationship between the severity of alcohol- and nicotine-dependency, which in turn, may be controlled by genetic factors. Some research suggests that smoking may reduce the intoxicating effects of alcohol, promoting the progression from moderate to heavy drinking.

In addition, laboratory findings show that regular alcohol use and heavy smoking are linked to an increased rate of alcohol elimination from the body. Alcohol is metabolized by the liver enzyme alcohol dehydrogenase. Alcoholics who smoke often have high blood levels of the liver enzymes aspartate aminotransferase (AST; also known as [serum] glutamic-oxaloacetic transaminase [SGOT]) and alanine aminotransferase (ALT; also known as [serum] glutamic-pyruvic transaminase [SGPT]). These enzymes are released into the blood because of liver damage caused by alcohol or other toxic substances.

Alcoholism also is associated with significant immune suppression—as shown by changes in the interferon system (class of antiviral proteins) and by the altered activity of natural killer cells (cells capable of producing cell-killing reactions). Therefore, a history of drinking alcohol may increase a person's susceptibility to carcinogenesis.

Asbestos

Researchers have found that there is a synergistic interaction between cigarette smoke and asbestos exposure. In a synergistic interaction, the combined effect of two or more agents is greater than that of either agent alone. It is estimated that asbestos workers with a history of cigarette smoking have a lung cancer risk that is eight times higher than smokers who have not been exposed to asbestos.

In addition, asbestos-exposed male smokers have roughly 50 times the lung cancer risk of unexposed men who do not smoke.

Asbestos-related diseases—whether expressed as lung cancer, asbestosis (asbestos-associated pneumoconiosis; dust-induced inflammatory disease of the lungs), or malignant mesothelioma (cancer of the mesothelium, a thin tissue that lines the body cavity)—usually develop more than 20 years after initial exposure. Plaques (surface patches) and thickening of the pleura (thin covering of the lungs) may indicate asbestos exposure, but they are not associated with an increased risk for lung cancer.

Similarly, fibrosis (formation of fibrous tissue as a repair process) does not accurately predict the development of lung cancer, since asbestos is associated with lung cancer even in the absence of lung fibrosis.

All histologic (tissue) types of lung cancer have been linked to asbestos exposure in smokers and nonsmokers. However, lung adenocarcinoma (gland-like type of lung cancer) may have more point mutations in a gene known as the K-ras oncogene (viral gene that can transform a host cell into a cancer cell) than other forms of lung cancer. Experts believe that if K-ras mutations are caused by smoking, asbestos may promote lung cancer by giving the mutated cells selective conditions for growth and expansion.

Diet and Body Mass

A number of studies suggest that there is a correlation between lung cancer risk and the dietary intake of cholesterol and/or fat. Some experts theorize that dietary fat consumption may actually modify the association between smoking and lung cancer in certain countries and subpopulations.

Researchers have found a relationship between the dietary intake of vegetables and a modest, protective effect against lung cancer. In particular, there may be an inverse association between the intake of beta-carotene, which is found in many yellow and green vegetables, and lung cancer risk. The anticarcinogenic (cancer-inhibiting) effect of beta-carotene seems most apparent among people who are at higher risk due to past or present smoking habits.

Beta-carotene may not be the only protective dietary substance. Some studies have indicated strong, protective effects from a diet that is high in all vegetables, cruciferous vegetables (e.g., cabbages, cauliflower), tomatoes, and other vegetable-based compounds, such as indoles, lycopene, lutein, vitamin E, and selenium.

One explanation for vegetables' protective effect is the scavenging of **free radicals** (elements or atoms that pass intact from one compound to another in a free state) by **antioxidants**, agents that stop the process of oxidation, thus preventing the breakdown of bodily substances. Beta-carotene, vitamin C, vitamin E, selenium, and other compounds are antioxidants that are found within vegetables and fruits. Studies of chemoprevention—cancer prevention by chemicals—are being conducted by the National Cancer Institute (NCI) and other agencies to determine the benefits, if any, of antioxidant supplements in people at high risk for lung cancer (e.g., smokers, asbestos-exposed workers).

Most studies have focused on the antioxidants beta-carotene and retinol. Unfortunately, researchers do not yet understand the nature of the association among dietary intake, blood levels of antioxidants, and lung cancer risk. A low blood level of beta-carotene may increase the risk for lung cancer, or it may be a marker of some other undetermined factor. Hopefully, data from ongoing chemoprevention trials will help to define this relationship.

A point of controversy is the inverse, or opposite, association between low body weight, or body mass index (BMI), and lung cancer. Some researchers have observed that thinness is related to increased lung cancer risk, regardless of smoking habits or weight loss due to disease. By contrast, other researchers suggest that the thinness/lung cancer association can be explained by smoking habits alone. More information is still needed to determine whether or not low body weight causes or reflects increased susceptibility to lung cancer, especially in smokers.

Environmental Tobacco Smoke (ETS)

Over the last several years, research has focused on the dangers of exposure to environmental tobacco smoke (ETS), also known as **secondhand smoke**, passive smoking, or involuntary smoking (i.e., breathing in the smoke from nearby smokers). It is estimated that approximately one-third of lung cancer in nonsmokers result from passive exposure to secondhand cigarette smoke.

ETS is made by the dilution of sidestream smoke from smoldering cigarettes and from the residues of mainstream smoke exhaled by active smokers. Research has shown that the smoke inhaled by nonsmokers is similar to that

inhaled by smokers, except that it has: **higher levels of some chemicals** known as nitrosamines and **smaller particle sizes**, leading to easier deposition within the bronchial tree. Specifically, smaller, ETS particles are more likely to reach and be held in the lungs, where they dissolve more readily than larger particles. Therefore, the pattern of deposition of smoke particles in the respiratory tract differs between active and passive smokers.

About 100 chemicals have been identified in sidestream smoke, although nearly 40 times that number have been detected in mainstream cigarette smoke. This difference occurs because of the extreme dilution of sidestream smoke. ETS is over 100,000 times more diluted than mainstream smoke, is less humid, and has very few volatile compounds. Since ETS is even more diluted than sidestream smoke, fewer than 20 ETS chemicals have been determined directly. Experts assume that the remaining substances in ETS are similar to those in sidestream smoke.

For general purposes, The U.S. Environmental Protection Agency (EPA) considers mainstream smoke, sidestream smoke, and ETS to be chemically similar.

Sidestream smoke contains some of the same toxic chemicals that are in mainstream smoke, which has over 40 established or suspected human carcinogens, including several known lung carcinogens. Some of the gas components of sidestream smoke are carbon dioxide, carbon monoxide, methane, acetylene, and nitrogen oxides. Some of the smoke particles include "tar," toluene, phenol, benzo(a)pyrene (BaP), methylquinolines, tobacco-specific nitrosamines (TSNAs), and nicotine.

Occupational Exposure

Occupational exposure—particularly uranium, radon, or asbestos exposure—can interact with smoking in an additive or synergistic manner. That is, lung cancer rates may be increased beyond the effects of either exposure alone. Therefore, it is essential to obtain an accurate occupational and smoking history when determining a person's risk for lung cancer.

A number of global committees have reviewed the cancer-causing potential of common occupational substances. For example, the International Agency for Research on Cancer (IARC) and the International Union Against Cancer (IARC) have identified many workplace materials that are possible lung carcinogens.

It is not known what percentage of all lung cancer is due to occupational exposure. This uncertainty is because information about workers' exposure is often incomplete or inaccurate. In addition, there is no histologic basis for distinguishing between lung cancers that are caused by occupational versus other factors. Yet, in spite of these limitations, some experts calculate that about 15 percent of lung cancers in men and 5 percent of lung cancers in women can be attributed to occupational exposure. Others estimate that occupation contributes to 1–5 percent of lung cancers in men and women of industrialized nations.

Radiation

Physicians have known for many years that uranium miners have a greatly increased rate of lung cancer. This increase is linked to the irradiation of lung tissue by uranium's decay product—radon (Rn) gas—and its decay products, which are known as radon "progeny" or radon "daughters." Therefore, there is concern that long-term exposure to radon in the home environment could pose a risk of lung cancer. Some experts believe that low exposures for prolonged time periods may be more hazardous than equivalent radon exposures received at higher levels for shorter periods.

Outdoors, the average level of radon gas in the air is about 0.2 picocurie per liter (pCi/L). In homes in the United States, radon levels range from a mean of about 1.25 pCi/L to a high of 100 pCi/L (very uncommon). The U.S. Environmental Protection Agency (EPA) has defined "high exposure" to radon as being 4 pCi/L and above. Many states (e.g., California, Louisiana, Oregon) have consistently low percentages of residential levels above 4 pCi/L,

whereas other states (e.g., Colorado, North Dakota) have many more homes with radon levels above 4 pCi/L. Most investigators agree that it is very difficult to determine the significance of radon in mixed smoking and nonsmoking populations, since the joint effect of radon and tobacco remains uncertain.

Other forms of radiation also are associated with lung cancer. For example, atomic bomb radiation is responsible for an increased risk of lung cancer among the exposed Japanese population. In addition, radiation therapy has caused an increased risk for lung cancer among British patients who received such treatment for ankylosing spondylitis and among smokers who have received radiation treatment for breast cancer and other disorders.

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