SECONDARY CANCERS: WHO IS AT RISK?

Learning about the risk of developing a second cancer can be frustrating and anxiety provoking. As people with cancer live longer, it becomes more important to study the long-term effects of cancer treatment. Of all the possible late complications of cancer treatment, developing a second cancer is one of the most serious.

People can have more than 1 cancer in their lifetime. Cancer is a very common disease. But not all second cancers are due to cancer treatment. For example, certain inherited gene changes can increase a woman's risk for both breast and ovarian cancer. Also, exposure to certain cancer- causing substances, like tobacco smoke, can put a person at risk for several different cancers, such as lung cancer and also cancers of the larynx, throat, or mouth. The National Cancer Institute has sponsored several clinical trials related to the long-term effects of cancer treatment. These are helping us to better understand how cancer treatments affect the development of second cancers.

WHO IS AT RISK FOR A SECOND CANCER?

People who received certain chemotherapy drugs. The risk of developing a secondary cancer is increased for people who were treated with high doses of alkylating agents such as:

- mechlorethamine
- chlorambucil
- cyclophosphamide (Cytoxan)
- melphalan
- semustine
- lomustine (CCNU)
- carmustine (BCNU)
- prednimustine
- busulfan
- dihydroxybusulfan

The risk gets higher with higher drug doses, longer treatment time, and higher dose-intensity (meaning that more drug is given over a short period of time). Studies have shown that leukemia risk begins to rise about 2 years after treatment with alkylating agents, becomes highest after 5 to 10 years, and then the risk decreases. Leukemia that develops after treatment with alkylating agents can be hard to treat and tends to have a poor outcome.

The chemotherapy drug cisplatin is not an alkylating agent, but it attacks cancer cells in much the same way. Cisplatin seems to increase the risk of

leukemia, too. This leukemia is hard to treat and tends to have a poor outcome, much like the leukemia linked to the alkylating agents. But the risk of developing leukemia after treatment with cisplatin is not as great as with the alkylating agents. Cisplatin is used to treat a lot of different cancers, including lung, testicular, and ovarian cancer. The risk of leukemia rises as the amount of drug used gets higher. The risk of developing leukemia increases even more if radiation is given along with the cisplatin.

In more recent years, drugs that are topoisomerase II inhibitors have also been found to cause leukemia, mainly AML. Drugs in this class include etoposide, teniposide, and mitoxantrone. Leukemia develops sooner after treatment with these drugs, than the leukemia from alkylating agents. Most cases are found within 2 or 3 years of treatment. Etoposide (VP-16, Etopophos, or Vepesid) is used to treat patients with non-small cell lung cancer, testicular cancer, and ALL and is linked with an increased risk of developing AML. Treatment of childhood ALL with teniposide is also thought to increase the risk of AML. Mitoxantrone (Novantrone), used to treat breast cancer and lymphoma, can also cause acute leukemia. Leukemia from these drugs acts differently from the leukemia from alkylating agents -- it responds to treatment better and has a better outlook.

More recently, evidence has suggested that the class of chemotherapy drugs called anthracyclines may also cause AML. Examples of anthracyclines include the drugs doxorubicin (Adriamycin), daunorubicin, and epirubicin (Ellence). These drugs are also topoisomerase II inhibitors, but are less likely to cause leukemia than etoposide, teniposide, and mitoxantrone.

People who received radiation therapy. Radiation therapy increases the risk of developing a secondary solid tumor as a person ages. The most common sites include the skin, breast, central nervous system (the brain and spine), thyroid gland, and bones. In contrast, other cancers, which are mostly solid tumors, have been shown to take much longer to develop. Most of these cancers are not seen for 10 years after radiation therapy and some are diagnosed even more than 15 years later. The effect of radiation on the risk of developing a solid tumor cancer depends on the dose of radiation, the area treated, and the age of the patient when they were treated with radiation.

In general, the risk of developing a solid tumor after radiation treatment goes up as the amount of radiation increases. The area treated is also important, since these cancers tend to develop in or near the area that was treated with radiation. For example, the risk of developing breast cancer after radiation is higher in those who were treated when they were young compared with those given radiation as adults. The chance of developing breast cancer after radiation seems to be highest in those exposed as children. Risk decreases as the age at the time of radiation increases, with little or no increase in breast cancer risk among women who had radiation after the age of 40. Age at the time of radiation treatment has a similar effect on the development of other solid tumors, including lung cancer, thyroid cancer, bone sarcoma, and gastrointestinal or stomach cancers.

Other factors can also influence the risk of radiation-related cancers. Smoking, for example, increases the risk of lung cancer after radiation even more. Early menopause can lower the risk of radiation-related breast cancer. For some cancers, the risk is higher if chemotherapy was given along with radiation.

More research will probably be done in the future on the interaction of genetics and radiation therapy and the link between radiation therapy and other cancer-causing agents.

People who have a history of cancer in the family. Some cancer patients have inherited gene changes (mutations) that increase the chances of getting a second cancer. But overall, these inherited changes are relatively uncommon and account for less than 10 percent of patients with cancer. Doctors suspect the presence of a cancer gene when a family history shows multiple cancers among young people in every generation, or when cancer occurs in both sides of paired organs (such as the eyes, breast, kidneys, etc.) If you have any questions or think that cancer may "run in your family" you should talk to your healthcare provider. A review of your family medical history will tell whether genetic counseling or testing is needed.

WHAT CAN I DO TO LOWER THE RISK OF GETTING A SECOND CANCER?

Avoid cancer promoting habits. Survivors should not smoke or chew tobacco and should avoid exposure to secondhand smoke when at all possible. Because skin cancers are one of the most common second cancers, especially for those treated with radiation therapy, you should take extra care to protect your skin from sun exposure. This includes regularly using sunscreen with sun protection factor (SPF) of 15 or more, wearing protective clothing, avoiding outdoor activities from 10am to 2pm when the sun's rays are most intense, and not tanning.

Drink alcohol only in moderation. Heavy drinkers, especially those who use tobacco, have a high risk of cancer of the mouth, throat, and esophagus. The risk of breast cancer may be increased in women who drink alcohol. Limiting the use of alcohol can reduce these cancer risks and decrease the chances of other alcohol-related problems, such as liver disease.

Eat right. A high intake of dietary fat has been linked to the risk of several common cancers. People who eat high-fat diets have a greater risk of getting colon cancer; this may also be true for breast and prostate cancers. To reduce all of these risks, daily fat intake should be limited to 30% or less of your total calories. Make sure to eat plenty of vegetables and fruits high in vitamins A and C such as dark green and deep yellow vegetables, citrus fruits and melons.

SUMMARY

The risk of second cancers must always be weighed against the benefits gained with treatment. The risks of treatments should always be compared carefully against the cost of not using such treatments. For many new cancer treatments, the long-term effects that cause second cancers are not yet known. The need for ongoing follow-up of cancer survivors is important so that we can better understand the long-term effects of cancer treatment.

Works Cited

Adapted from the American Cancer Society
www.cancer.org

Adapted from the Children's Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers
www.survivorshipguidelines.org