Second Cancers in Adults

This document focuses on second cancers in adults. For information about second cancers after treatment of childhood cancers, see our document *Children Diagnosed With Cancer: Late Effects of Cancer Treatment*.

What are second cancers?

Advances in early detection and treatment mean that more and more people are surviving cancer today. Cancer survivors can be affected by a number of health problems, but often their greatest concern is facing cancer again. If a cancer comes back after treatment it is called a “recurrence.” But some cancer survivors may develop a new, unrelated cancer later. This is called a “second cancer.” No matter what type of cancer you have had, it is still possible to get another (new) cancer, even after surviving the first.

For people with some types of cancer, the risk of getting certain other types of cancer is clearly higher, but for other types it’s not as clear if the risk is increased. Because it can take many years for cancers to develop, second cancers have been studied best in types of cancers for which successful treatments have been around the longest. That’s why we know more about second cancers after certain types of cancer than for others..

Often, second cancers seem to happen more often than would be expected just based on how common cancer is. Sometimes the new cancer is in the same organ as the first. For example, someone who was treated for colon cancer can get another colon cancer. Others occur in other organs or tissues.

What causes second cancers?

It isn’t always clear what causes second cancers. Some seem to be caused by the same things that caused the first cancer. Others may be caused by cancer treatment.

How do shared risk factors affect the risk of second cancers?

For some cancers, having that cancer means you are at an increased risk of getting another cancer in the same organ or nearby. This may be because the whole organ (and sometimes nearby organs and tissues) were exposed to the same cancer-causing agents that led to the first cancer. This

means that the entire area could already have early changes that can lead to cancer. This is called *field cancerization*.

Field cancerization is one reason people might get a second cancer near the same area, such as a second colorectal cancer, breast cancer, lung cancer, bladder cancer, or head and neck cancer.

Shared environmental risk factors

For some cancers, the agent that caused the cancer isn't always obvious. For example, although there are many risk factors for colorectal and breast cancer, many cases have no clear cause.

For others, the cancers can be linked to things known to cause cancer, like smoking, alcohol, or HPV (human papilloma virus) infection. For example, cancer of the larynx (voice box) is often caused by smoking. But the larynx isn't the only part of the body exposed to cigarette smoke, so it isn't surprising that people who have had cancer of the larynx also have a higher risk of other smoking-related cancers, such as cancer of the mouth, throat, esophagus (tube connecting the throat to the stomach), and lung.

Sometimes the second cancer isn't nearby, but is still linked to the same cancer-causing agent. For example, bladder cancer can be caused by smoking. People who have had bladder cancer have an increased risk of some other cancers linked to smoking, such as cancers of the lung and larynx.

Genes and family cancer syndromes

In some people, their cancer is linked to a family cancer syndrome. These syndromes are caused by abnormal gene changes (mutations) that are often inherited from a parent. Family cancer syndromes are often linked to increased risks of more than one kind of cancer. For example, women with hereditary breast and ovarian cancer syndrome, which is linked to mutations in the genes *BRCA1* and *BRCA2*, have a high risk of both breast, ovarian, and some other cancers. Hereditary non-polyposis colorectal cancer syndrome, also known as Lynch syndrome, is linked to a high risk of colorectal, endometrial, bladder, and some other cancers.

How does radiation therapy affect the risk of second cancers?

Radiation therapy was recognized as a potential cause of cancer many years ago. In fact, much of what we know about the possible health effects of radiation therapy has come from studying survivors of atomic bomb blasts in Japan. We also have learned from workers in certain jobs that included radiation exposure, and patients treated with radiation therapy for cancer and other diseases.

How does radiation affect the risk of leukemia and myelodysplastic syndrome?

Most kinds of leukemia, including acute myelogenous leukemia (AML), chronic myelogenous leukemia (CML), and acute lymphoblastic leukemia (ALL) can be caused by past radiation exposure. Myelodysplastic syndrome (MDS), a bone marrow cancer that can turn into acute

leukemia, has also been linked to past radiation exposure. The risk of these diseases after radiation treatment depends on a number of factors such as:

- How much of the bone marrow was exposed to radiation
- The amount of radiation that reached the bone marrow
- The radiation dose rate (how much was given in each dose, how long it took to give the dose, and how often it was given)

The person's age when they were treated with radiation does not seem to be a risk factor. Most often, these cancers develop within several years of radiation treatment, peaking at 5 to 9 years after exposure. Then the number of new cancers slowly declines over the following years.

How does radiation affect the risk of solid tumors?

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 at least 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 such factors as:

- The dose of radiation
- The area treated
- 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 dose of radiation increases. Some cancers require larger doses of radiation than others, and certain treatment techniques use more radiation.

The area treated is also important, since these cancers tend to develop in or near the area that was treated with radiation. Certain organs, such as the breast and thyroid, seem to be more likely to develop cancers after radiation than others.

Age at the time of treatment also affects the risk of solid tumors. 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 affect the risk of radiation-related cancers. Smoking, for example, increases the risk of lung cancer after radiation even more. Early menopause, which can be caused by chemotherapy, can lower the risk of radiation-related breast cancer. For some cancers though, the risk is higher if chemotherapy was given along with radiation.

Future research will look at how genetics and radiation therapy interact, as well as the link between radiation therapy and other cancer-causing agents.

How does chemotherapy affect the risk of second cancers?

Some types of chemotherapy (chemo) drugs have been linked with different kinds of cancer. The cancers most often linked to chemo are myelodysplastic syndrome (MDS) and acute myelogenous leukemia (AML). Sometimes, MDS occurs first, then turns into AML. Acute lymphocytic leukemia (ALL) has also been linked to chemo. Chemo is known to be a greater risk factor than radiation therapy in causing leukemia.

Some solid tumor cancers have also been linked to chemo treatment for certain cancers, such as testicular cancer.

Alkylating agents

Alkylating agents are chemo drugs that interfere with a cell's DNA in a certain way. These drugs can sometimes cause AML and MDS. Often MDS develops first, which then progresses to AML.

Alkylating agents known to cause leukemia include:

- Mechlorethamine
- Chlorambucil
- Cyclophosphamide (Cytoxan®)
- Melphalan
- Lomustine (CCNU)
- Carmustine (BCNU)
- Busulfan

The risk gets higher with higher drug doses, longer treatment time, and higher dose-intensity (more drug 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 declines.

Unfortunately, MDS and leukemia that develop after treatment with alkylating agents tend to be hard to treat and have a poor outcome.

Cisplatin and carboplatin

The chemo drugs cisplatin and carboplatin are not an alkylating agents, but they attack cancer cells in much the same way. These drugs seem to increase the risk of leukemia (mainly AML), too, but the risk is not as great as with the alkylating agents. This leukemia is hard to treat and tends to have a poor outcome, much like the leukemia linked to the alkylating agents.

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 cisplatin or carboplatin.

Topoisomerase II inhibitors

The class of chemo drugs called *topoisomerase II inhibitors* stop cells from being able to repair DNA. These drugs can also cause leukemia, mainly AML.

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 and without MDS occurring first.

Drugs in this class include

- Etoposide (VP-16)
- Teniposide
- Mitoxantrone (Novantrone®)

Drugs called *anthracyclines* are also topoisomerase II inhibitors. Anthracyclines are less likely to cause leukemia than the other topoisomerase II inhibitors. Examples of anthracyclines include:

- Doxorubicin (Adriamycin®)
- Daunorubicin
- Epirubicin (Ellence®)
- Idarubicin

Leukemia from topoisomerase II inhibitors tends to respond to better to treatment and has a better outlook than the leukemia from alkylating agents.

Targeted therapy drugs

Some drugs used to treat cancer are called targeted therapy drugs because they were designed to fight cancer by targeting certain genes or proteins.

Vemurafenib (Zelboraf®) and dabrafenib (Tafinlar®) are drugs that target the BRAF protein. They are used to treat melanoma and are being studied for use in other cancers. People taking these drugs have a higher risk of squamous cell carcinomas of the skin.

How do stem cell transplants affect the risk of second cancers?

Stem cell transplants involve treatment with high doses of chemotherapy, sometimes with radiation, followed by an infusion of blood stem cells to restore the bone marrow. The stem cells can be from a donor (called an allogeneic transplant) or the patient’s own cells that were collected earlier (an autologous transplant). Because the donor cells could see the patient’s cells as foreign and attack them, patients who get allogeneic transplants need to be treated with drugs to suppress the immune system.

Any kind of stem cell transplant is linked to an increased risk of second cancers from the chemotherapy and radiation used.

Patients who get allogeneic transplants also have a risk of developing a post-transplant lymphoproliferative disorder (PTLD), an out-of-control growth of lymph cells. PTLD is often linked to a malfunction of one type of lymph cell, the T-cell, and the presence of Epstein-Barr virus (EBV) in another type of lymph cell called the B-cell. When the T-cells aren't working well, EBV-infected B-cells can grow and multiply. This disorder can range from a benign increase in lymphocytes in lymph nodes and bone marrow to lymphoma. More information about PTLD can be found in our document *Stem Cell Transplant (Peripheral Blood, Bone Marrow, and Cord Blood Transplants).*

Graft-versus-host disease (GVHD) can happen in allogeneic transplants when the immune cells from the donor see the recipient's body as foreign. The donor immune cells may attack certain organs, most often the skin, gastrointestinal (GI) tract, and liver. Patients with chronic GVHD have an increased risk of squamous cell cancers of the skin and head and neck.

Can I lower my risk of getting a second cancer?

Some people might think that if they've had cancer, the odds are that they won't get another one. But people who have had cancer are often at increased risk for some other types of cancer. And even if they're not at increased risk, they still have the same risks for other types of cancers as do all other people.

It's very important that people who have had cancer understand what their risks are. If you've had cancer, talk with your doctor about what other cancers you might need to watch out for more closely. Ask if there are things you can do that might lower your risk, or if there are screening tests you should have to look for cancer early.

If you have completed treatment, be sure to keep any follow up appointments. Let your doctor know if you have any new symptoms or problems, because they could be caused by the cancer coming back or by a new disease or cancer. Survivors should also continue to follow the American Cancer Society guidelines for the early detection of cancer.

To help maintain good health, survivors should also:

- Achieve and maintain a healthy weight
- Adopt a physically active lifestyle
- Consume a healthy diet, with an emphasis on plant foods
- Limit consumption of alcohol to no more than 1 drink per day for women or 2 per day for men
- Stay away from tobacco

These steps may also lower the risk of some cancers.

For more information about follow-up care and second cancers after treatment for specific types of cancer, see our detailed guides for each cancer type.

Additional resources

More information from your American Cancer Society

We have some related information that may also be helpful to you. These materials may be ordered from our toll-free number, 1-800-227-2345.

Childhood Cancer: Late Effects of Cancer Treatment

A Guide to Chemotherapy (also available in Spanish)

A Guide to Radiation Therapy (also available in Spanish)

Stem Cell Transplant

Family Cancer Syndromes

No matter who you are, we can help. Contact us anytime, day or night, for cancer-related information and support. Call us at **1-800-227-2345** or visit www.cancer.org.

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Last Medical Review: 12/11/2014
Last Revised: 12/11/2014

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