

Second Cancers Caused by Cancer Treatment

Advances in radiation therapy and chemotherapy have increased the chances of survival for many people with cancer today. People with cancer are often living longer, so it's becoming 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 one cancer in their lifetime. Cancer is a very common disease, and 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, being exposed to certain cancer- causing substances, like tobacco smoke, can put a person at higher risk for several different cancers, such as cancers of the lung, larynx (voice box), throat, and mouth. Even though it is hard to separate out the exact cause of any one person's cancer, here we will try to focus on the risk of second cancers that may be linked to past cancer treatment.

Treatments linked to the development of second cancers

Radiation therapy

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.

Leukemia

Acute myelogenous leukemia (AML), chronic myelogenous leukemia (CML), and acute lymphoblastic leukemia (ALL) have been linked to past radiation exposure.

Myelodysplastic syndrome (MDS), a bone marrow disorder 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 active 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 cases usually develop within several years of radiation treatment, peaking at 5 to 9 years after exposure. Then the number of cases developing slowly declines over the following years.

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 techniques require more radiation. For example, intensity modulated radiation therapy (IMRT) helps to protect tissues that are more easily injured by radiation, but a larger dose of radiation overall must be used.

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

Chemotherapy

The cancer most often linked to chemotherapy (chemo) as the cause is acute myelogenous leukemia (AML). In many cases, myelodysplastic syndrome (MDS), a bone marrow problem that is sometimes called a type of cancer, occurs first, then turns into AML. Acute lymphocytic leukemia (ALL) has also been linked to chemo. Chemo is known to be a higher 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

Certain types of chemo drugs called *alkylating agents* have been shown to increase the risk of AML when used to treat certain cancers like Hodgkin disease, non-Hodgkin lymphoma (NHL), ovarian, lung, and breast cancer.

Alkylating agents known to cause leukemia include:

- 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 doseintensity (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 declines. Alkylating agents often cause MDS first, which then progresses into an acute leukemia. MDS and leukemia that develop after treatment with alkylating agents can be hard to treat and tends to have a poor outcome. Often,

Cisplatin

The chemo 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.

Topoisomerase II inhibitors

In more recent years, a class of chemo drugs called *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 lung cancer, testicular cancer, ALL, and other cancers, 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, lymphoma, and other cancers, can also cause acute leukemia.

Leukemia from these drugs acts differently from the leukemia from alkylating agents – it tends to respond to treatment better and has a better outlook. Also, these drugs don't often cause MDS first.

Anthracyclines

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.

Cancers linked to the development of second cancers

No matter what type of cancer is treated, treatments such as radiation and chemotherapy can lead to a second cancer in the long run. Because it can take many years for treatmentrelated cancers to develop, they have been studied best in those who have lived a long time after being treated. Successfully treating a first cancer gives a second cancer the time (and the chance) to develop. The cancers discussed in this section were some of the first cancers in which treatment led to long-term survival. It is likely that we will see second cancers developing after some other cancers as treatment and survival improves.

Hodgkin disease

Survivors of Hodgkin disease (HD) have a risk of developing another cancer that is 2 to 3 times that of people who didn't have HD (the general population). Overall, the risk of a second cancer is more than 20% (1 in 5) in the first 20 years after treatment.

Risk of leukemia

Survivors of HD have an increased risk of acute leukemia and myelodysplastic syndrome (MDS) that is mainly linked to treatment with chemotherapy (chemo). The risk with chemo is highest if an alkylating agent was used, particularly when the combination of drugs known as MOPP (mechlorethamine, vincristine/Oncovin, prednisone, and procarbazine) was used as the main chemo regimen. Leukemia and MDS are much less common in people treated with regimens that include the combination known as ABVD (doxorubicin/Adriamycin, bleomycin, vinblastine, and dacarbazine).

Some patients with HD are treated with stem cell transplant. Most often, this is used for HD that has come back after treatment (or never went away in the first place). Patients with HD treated with stem cell transplant have a higher risk of leukemia and MDS that seems to be related to the additional chemo that is given prior to transplant.

Treating HD with radiation alone has little effect on leukemia risk, but adding radiation to chemo may increase the risk from the chemo even further.

The chance of getting leukemia after HD is related to the patient's age when they were treated, with the highest risk seen in those who were 35 or older during treatment. The risk also seems to go up as the amount of chemo used increases.

Risk of non-Hodgkin lymphoma

The risk of non-Hodgkin lymphoma (NHL) is also higher in those who survive HD. Because this risk does not seem to change based on the type of treatment used, many experts do not think that NHL seen after HD is caused by cancer treatments.

Risk of solid tumors

Radiation therapy for HD has been linked to an increased risk of developing solid tumor cancers. The risk is highest in the parts of the body that were in the path of the radiation beam.

The most common second cancer in female survivors of HD is breast cancer. The risk is highest in those who had radiation to an area in the center of the chest between the lungs before age 30. In the past, many patients got radiation to this area as a part of *mantle field* radiation. (Mantle field radiation covers the area of the neck, chest, and armpits.) The risk of breast cancer from radiation can be affected by chemo and its side effects. Alkylating agent chemotherapy causes some women to go through menopause early. In women who went through menopause before age 35 because of HD treatment, the risk of breast cancer isn't increased – it's actually lower than expected.

Lung cancer risk is also higher after treatment for HD. This higher risk is related to chest radiation treatments as well as chemotherapy with alkylating agents. Patients who have both chemo and radiation are even more likely to develop lung cancer. Smoking further increases the risk. The risk of lung cancer goes up if the patient smoked before treatment, but the risk gets even higher if the patient keeps on smoking after treatment.

The risk of thyroid cancer is also increased in HD patients who were treated with radiation to the neck. Other cancers that are seen after radiation include gastrointestinal (stomach) cancer and sarcoma.

Over time, treatment for HD has changed. Chemotherapy with alkylating agents has become much less common. Radiation is given in lower doses, and often only the areas directly affected by HD are treated (known as *involved-field radiation*). These changes seem to have helped lower the cancer risks after treatment, but long-term follow-up studies are still needed.

Follow-up care

Since there is an increased risk for a second cancer following treatment for Hodgkin disease, survivors of HD should be carefully followed up. Your doctors should watch for the development of solid tumors, leukemia, and non-Hodgkin lymphoma along with recurrence of Hodgkin disease.

All patients should be encouraged to reduce their risk of lung cancer by avoiding tobacco smoke.

Women who were treated with radiation to the chest (such as mantle field radiation therapy) before age 35 should start breast cancer screening early. The Children's Oncology Group's guidelines recommend that patients treated with this type of radiation (as a child, teen, or young adult) start screening 5 to 8 years after finishing their HD treatment or at age 25, whichever is later. This screening should include regular breast exams, mammograms, and breast MRI. The American Cancer Society's guidelines

recommend yearly breast MRIs in addition to mammograms for women who were treated with chest radiation while they were aged 10 to 30.

Patients who had radiation to their abdomen (belly) should pay special attention to any abdominal problems and report them to the doctor right away. Problems like unplanned weight loss, ongoing diarrhea, or other bowel problems could be a sign of a serious condition.

Non-Hodgkin lymphoma

Survivors of non-Hodgkin lymphoma (NHL) are at increased risk of developing some second cancers, but less so than patients who were treated for Hodgkin disease. Overall, NHL survivors get new cancers about 15% more often than most people (the general population).

Survivors of NHL are at risk for several cancers such as:

- Melanoma (a type of skin cancer)
- Lung cancer
- Kidney cancer
- Kaposi sarcoma
- Cancers of the head/neck area (includes the lip, tongue, floor of the mouth, throat, salivary glands, and voice box)
- Colon cancer
- Thyroid cancer
- Bone and soft tissue cancer
- Bladder cancer
- Leukemia and myelodysplastic syndrome
- Hodgkin disease

Radiation therapy to the chest increases the risk of breast cancer in women who were treated before age 30. Mesothelioma, a rare cancer of the outer lining of the lung, is also increased in those who were treated with radiation.

A higher risk of bladder cancer has only been seen in those who were treated with chemotherapy. The drug cyclophosphamide (Cytoxan[®]), especially if used in higher doses, is linked to bladder cancer.

Low-dose total body irradiation (TBI), which was once used to treat NHL, has been linked to an increased risk of leukemia. The risk of leukemia is also higher in those treated with chemotherapy, with the highest risk seen in those treated with both radiation and chemotherapy. Patients who had autologous bone marrow transplants (meaning the patient's own bone marrow was used – not someone else's) are also at increased risk for developing acute myelogenous leukemia (AML) and myelodysplastic syndrome (MDS). This may be related to the chemo given before transplant.

Treatment-related second cancer risk after NHL increases over time. Those who were diagnosed and treated at younger ages (20 years old and younger) are more likely to develop a second cancer than those who were older (70 or older) when they were found to have NHL.

Follow-up care

Since there is an increased risk for a second cancer following treatment for NHL, survivors should get careful follow-up. Your doctors should be looking for the development of any of the above mentioned cancers as well as the recurrence of NHL.

All patients should be encouraged to avoid tobacco smoke.

Women who were treated with chest radiation prior to the age of 30 have an increased risk of breast cancer and should consider beginning breast screening at an early age. The Children's Oncology Group's guidelines recommend that patients treated with radiation to the chest (as a child, teen, or young adult) start screening 5 to 8 years after finishing their treatment or at age 25, whichever is later. This screening should include regular breast exams, mammograms, and breast MRI. The American Cancer Society's guidelines recommend yearly breast MRIs in addition to mammograms for women who were treated with chest radiation while they were aged 10 to 30.

Prostate cancer

Men whose prostates have been removed or destroyed with radiation can no longer get a new case of prostate cancer, but they can get recurrence of the original prostate cancer (the cancer can come back after treatment).

Men who are treated with radiation therapy have a higher risk of bladder cancer later on than men who had surgery to remove their prostates. They may also have a higher risk for colon and rectal cancer. This increased risk is mainly seen in men who were treated with external beam radiation therapy (EBRT). Men who had seed implants (brachytherapy) without EBRT may have a slightly increased risk of these cancers, but it is lower than what is seen with EBRT. Overall, the risk seen with radiation therapy is not high, but it can continue for more than 10 years after treatment.

The risk is likely related to the dose of radiation, as it is with other cancers. Men who get seed implants typically get less radiation to nearby organs than those who get EBRT, either by itself or along with seeds.

Newer methods of giving EBRT, such as intensity modulated and conformal beam radiation therapy, may have different effects on the risks of a second cancer. Because these methods are newer, the long-term effects have not been studied as well.

Some studies looking at the long term effects of prostate cancer treatment have found an increased risk of melanoma (a type of skin cancer) after radiation therapy, but this higher risk was seen after prostatectomy (surgery to remove the prostate) as well.

At one point, high doses of the female hormone estrogen were used to treat advanced prostate cancer. This was linked to breast cancer in some men. Estrogen is no longer a standard treatment for prostate cancer.

Follow-up care

Survivors who are treated with radiation have an increased risk of certain second cancers, so they should get careful follow-up. There are no special recommendations for watching for second cancers after prostate treatment at this time, although men who have had radiation to treat prostate cancer should be careful to follow screening recommendations for colorectal cancer to improve the chance of early detection. Your doctor will also be watching closely for recurrence of the prostate cancer. You should also report problems passing urine, blood in your urine, rectal pain, or rectal bleeding to your doctor right away.

All patients should be encouraged to avoid tobacco smoke. Men who smoke may further increase their risk of bladder cancer after prostate radiation, since smoking is a known risk factor for bladder cancer.

Testicular cancer

The most common cancer seen in testicular cancer survivors is a second testicular cancer. Overall, 2% to 5% of men who have had cancer in 1 testicle will eventually have it in the other testicle. The second cancer is not from treating the first cancer with radiation or chemotherapy. In fact, those treated with surgery alone still have an increased risk of a second testicular cancer. The chance of getting a second testicular cancer is actually lower in men who were treated with chemotherapy. The rest of this section is about second cancers other than testicular cancer.

Risk of solid tumors

Compared with most men in the general population, testicular cancer survivors are up to twice as likely to develop a new cancer outside the testicle. The chance of a second cancer changes over time and depends on which treatments were used and how old the patient was when he was treated.

The risk of a solid tumor cancer starts going up within 5 years and doubles after 10 years in those men who were treated with radiation alone. The risk is highest for cancers in the area that received radiation (the radiation field). This risk remains high and doesn't seem to go down with time.

The most common cancers seen after abdominal radiation for testicular cancer are cancers of the bladder, colon, pancreas, and stomach. Radiation to the abdomen also increases the risk of cancers of the rectum, kidney, and prostate. If the radiation field

includes the chest, the risks of lung cancer, esophagus cancer, mesothelioma (cancer of the outer lining of the lung), and thyroid cancer are increased. Radiation treatments also increase the risk of melanoma skin cancer and connective tissue cancer (sarcoma). The risks are generally greater with higher radiation doses or if the patient got both chemotherapy and radiation.

In recent years, radiation therapy for testicular cancer has changed. Lower doses of radiation are used, and preventive treatment to the chest has been stopped. Long-term follow-up studies are needed to see if these changes have lowered the cancer risks.

Chemotherapy is linked with an increased risk of solid tumor cancers that is slightly less than what is seen after radiation.

Risk of leukemia

The risk of leukemia (and myelodysplastic syndrome or MDS) after treatment for testicular cancer is also increased. Use of the chemotherapy drug cisplatin is linked most often to leukemia and MDS, although high doses of etoposide (VP-16, Etopophos[®], or Vepesid[®]) are sometimes also a factor (doses higher than what are normally used today). Radiation given with chemotherapy seems to increase risk even more. Leukemia and MDS are both uncommon cancers normally, so even though the risk of these cancers is higher than average, very few patients develop them from their treatment.

Follow-up care

Standard follow-up for survivors of testicular cancer includes frequent doctor visits, exams, and imaging tests for a number of years. Over time, follow-up becomes less intense, but they should see a doctor at least once a year or sooner if any problems develop.

Because the most common cancer seen is a second testicular cancer, survivors should perform regular testicular self-exams.

All patients should be encouraged to avoid tobacco smoke.

Ovarian cancer

The increased risk of second cancers in ovarian cancer survivors includes cancers of the colon, rectum, small intestine, renal pelvis, breast, bladder, and bile duct, melanoma of the eye, and leukemia.

Radiation therapy is linked with cancers of connective tissues, bladder, and possibly pancreas cancer.

Chemotherapy is linked with an increased risk for leukemia. The main drugs linked with leukemia risk are platinum agents (like cisplatin and carboplatin). The risk increases as the total dose of these drugs increases, but the overall risk is still low.

Genetic factors that may have caused ovarian cancer in the first place may also add to the risk of breast and colorectal cancers. For example, women with mutations in the *BRCA* genes have a high risk of both ovarian and breast cancer, as well as some other cancers. Women with the inherited disorder called hereditary non-polyposis colorectal cancer (HNPCC, also called Lynch syndrome), have a high risk of colon, rectum, and small intestine cancers, as well as ovarian and other cancers.

Other risk factors for ovarian and breast cancer that overlap may also help explain some of the increased risk of breast cancer in ovarian cancer survivors.

Studies have shown that the risk of developing solid tumors is higher during all follow-up periods after ovarian cancer.

Follow-up care

Women who have had ovarian cancer will be watched closely for signs that the cancer has come back with regular physical exams, blood tests, and, sometimes, CT scans. These women have an increased risk of breast and colorectal cancers and should have regular screening for these cancers.

All patients should be encouraged to avoid tobacco smoke.

Breast cancer

Women with breast cancer are at a 3-to 4-fold increased risk of developing a new primary cancer in the opposite breast. Increased risk is also seen for cancers of the ovary, uterus, lung, colon, rectum, and connective tissue, as well as melanoma and leukemia. But for some of these cancers, such as cancer of the opposite breast, ovary, and uterus, the second cancer may be linked to the same thing that caused the first cancer, like genetics or a hormonal risk factor.

The most common second cancer seen in survivors of breast cancer is another breast cancer. Women who were treated with breast-conserving surgery (such as a lumpectomy) can develop a cancer in the same breast, but anyone can get a new cancer in the other breast. The risk of a second breast cancer is high no matter what treatment is used for the first cancer. Even women who receive no radiation or chemotherapy have an increased risk of cancer in the opposite breast. This increase in risk also shows up in close relatives of women with breast cancer, so there may be a shared pre-existing factor causing the first and second breast cancers in many of these women. Still, depending on the patient's age when they were treated, radiation therapy can increase the risk even more. Radiation therapy does not seem to increase the risk of cancer in the opposite breast if the patient is past the age of 45 at the time of treatment. But in women who had radiation therapy before the age of 45, an increased risk is seen 10 years after treatment.

The risk of lung cancer is also increased in women who had radiation therapy for breast cancer. The higher lung cancer risk is first seen 10 years after radiation, and gets higher over time. The risk of lung cancer after radiation is even higher in women who smoke.

Radiation therapy to the breast also increases the risk of sarcomas of blood vessels (angiosarcomas), bone (osteosarcomas), and other connective tissues. These cancers are most often seen in the remaining breast area, chest wall, or in the arm that had been treated with the radiation therapy. This risk remains high even 30 years after treatment.

Taking tamoxifen for 5 years not only makes it less likely that the breast cancer will come back, it also helps to lower the risk of breast cancer in the opposite breast by half. This appears to be true for women who have been followed for 10 years after their first treatment. But tamoxifen increases the risk for endometrial cancer in 5-year and 10-year survivors. Still, the benefits of treatment for breast cancer are greater than the risk of a second cancer.

There is a small risk of developing leukemia after treatment for breast cancer. The risk is highest when both chemotherapy and radiation therapy are given, especially if the chemotherapy includes an alkylating agent (see the list of alkylating agents above). Cyclophosphamide (Cytoxan[®]), an alkylating agent, has been used for over 30 years to treat breast cancer. It is a part of the regimen known as CMF (cyclophosphamide, methotrexate, and 5-FU), and is also included in the regimens AC (Adriamycin[®] [doxorubicin] and cyclophosphamide) and FAC (adds 5-FU to the drugs in AC). Studies have shown that higher doses of cyclophosphamide increase the risk of developing AML. The dose of cyclophosphamide that is now used in standard CMF and AC is linked with a low risk of leukemia. The risk also goes up with dose intensity (when a higher amount of drug is given over a shorter amount of time). Still, even with a risk of leukemia that is several times higher than what is usually seen, the leukemia risk even with high doses is only about 1%.

Follow-up care

Even women who were not treated with radiation have an increased risk of a second breast cancer in the opposite breast. Follow-up care should include annual screening for breast cancer (if there is any remaining breast tissue). Good gynecologic care is also important to watch for endometrial cancer.

All patients should be encouraged to avoid tobacco smoke.

Cervical cancer

Cervical cancer is often caused by infection with human papilloma virus (HPV). Survivors of cervical cancer have an increased risk for other HPV-related cancers, including cancers of the throat, anus, vulva, and vagina. Smoking is also linked to cervical cancer, and survivors of cervical cancer also have an increased risk of some cancers linked to smoking, such as lung cancer, bladder cancer, and pancreatic cancer.

The risks of bladder and lung cancer are even higher in those women who were treated with radiation. Radiation for cervical cancer also increases the risk of cancers of the colon, rectum, small intestine, uterus, ovary, kidney, soft tissue, and stomach. Radiation is also linked to a higher risk of acute leukemia and non-Hodgkin lymphoma.

Follow-up care

Survivors of cervical cancer need good gynecologic care to watch for signs of a new cancer in the vulva or vagina, as well as to watch for relapse.

All patients should be encouraged to avoid tobacco smoke.

Childhood cancers

As treatment for childhood cancer has improved and more children are surviving into adulthood, researchers have learned that the effects of treatment may affect the child's health later in life. This result, known as a "late effect," often includes an increased risk for some types of cancer. For more information about this topic, see our document, *Childhood Cancer: Late Effects of Cancer Treatment*. If you'd like this information, please call our 24-hour number 1-800-227-2345, or search for it on our Web site at www.cancer.org.

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 treatments.

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

Understanding Chemotherapy: A Guide for Patients and Families (also available in Spanish)

Understanding Radiation Therapy: A Guide for Patient and Families (also available in Spanish)

Surgery (also available in Spanish)

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.

References

Aisenberg AC. Problems in Hodgkin's disease management. Blood. 1999;93:761-779.

Bertelsen L, Mellemkjaer L, Christensen J, Rawal R, Olsen JH. Age-specific incidence of breast cancer in breast cancer survivors and their first-degree relatives. *Epidemiology*. 2009;20:175-180.

Boice JD Jr, Harvey EB, Blettner M, Stovall M, Flannery JT. Cancer in the contralateral breast after radiotherapy for breast cancer. *N Engl J Med.* 1992;326:781-785.

Bostrom PJ, Soloway MS. Secondary cancer after radiotherapy for prostate cancer: should we be more aware of the risk? *Eur Urol*. 2007;52:973-982.

Brown LM, Chen BE, Pfeiffer RM, et al. Risk of second non-hematological malignancies among 376,825 breast cancer survivors. *Breast Cancer Res Treat*. 2007;106:439-451.

Chaturvedi AK, Engels EA, Gilbert ES, et al. Second cancers among 104760 survivors of cervical cancer: evaluation of long-term risk. *J Natl Cancer Inst.* 2007;99:1634-1643.

Chaturvedi AK, Kleinerman RA, Hildesheim A, et al. Second cancers after squamous cell carcinoma andadenocarcinoma of the cervix. *J Clin Oncol*. 2009 Feb 20;27(6):967-73.

Children's Oncology Group. Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent and Young Adult Cancers. Accessed at www.survivorshipguidelines.org/pdf/LTFUGuidelines.pdf on 12/20/11.

Hemminki K, Lenner P, Sundquist J, Bermejo JL. Risk of subsequent solid tumors after non-Hodgkin's lymphoma: effect of diagnostic age and time since diagnosis. *J Clin Oncol*. 2008;26:1850-1857.

Karlsson CT, Malmer B, Wiklund F, Grönberg H. Breast cancer as a second primary in patients with prostate cancer--estrogen treatment or association with family history of cancer? *J Urol*. 2006;176:538-543.

Kry SF, Salehpour M, Followill DS, et al. The calculated risk of fatal secondary malignancies from intensity-modulated radiation therapy. *Int J Radiat Oncol Biol Phys.* 2005;62:1195-1203.

Moon K, Stukenborg GJ, Keim J, Theodorescu D. Cancer incidence after localized therapy for prostate cancer. *Cancer*. 2006;107:991-998.

Mudie NY, Swerdlow AJ, Higgins CD, et al. Risk of second malignancy after non-Hodgkin's lymphoma: a British Cohort Study. *J Clin Oncol*. 2006;24:1568-1574.

Ng AK, Travis LB. Subsequent malignant neoplasms in cancer survivors. *Cancer J.* 2008 Nov-Dec;14(6):429-34.

Nieder AM, Porter MP, Soloway MS. Radiation therapy for prostate cancer increases subsequent risk of bladder and rectal cancer: a population based cohort study. *J Urol.* 2008;180:2005-2009; discussion 2009-10.

Richiardi L, Scélo G, Boffetta P, et al. Second malignancies among survivors of germcell testicular cancer: a pooled analysis between 13 cancer registries. *Int J Cancer*. 2007;120:623-631.

Smith RE, Bryant J, DeCillis A, Anderson S. Acute myeloid leukemia and myelodysplastic syndrome after doxorubicin-cyclophosphamide adjuvant therapy for operable breast cancer: the National Surgical Adjuvant Breast and Bowel Project Experience. *J Clin Oncol.* 2003;21:1195-1204.

Travis LB. The epidemiology of second primary cancers. *Cancer Epidemiol Biomarkers Prev*. 2006;15.

Travis LB, Fosså SD, Schonfeld SJ, McMaster ML, et al. Second cancers among 40,576 testicular cancer patients: focus on long-term survivors. *J Natl Cancer Inst.* 2005;97:1354-1365.

Travis LB, Hodgson D, Allan JM, Van Leeuwen FE. Second Cancers. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *Cancer: Principles & Practice of Oncology*. 8th edition. Philadelphia: Lippincott William & Wilkins: 2008:2718-2743.

Tward JD, Wendland MM, Shrieve DC, Szabo A, Gaffney DK. The risk of secondary malignancies over 30 years after the treatment of non-Hodgkin lymphoma. *Cancer*. 2006;107:108-115.

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