

Long-Term Follow-Up Study

UNIVERSITY OF MINNESOTA
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From the editor

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In this issue: This issue of our newsletter focuses on therapy-related cancers that may occur in people treated in childhood for cancer, leukemia, tumor, or similar illness. On page two you will find a summary of what we have learned about these cancers among the members of our cohort. On page three Dr. Melissa Hudson, one of our investigators, offers some reflections to put these findings into perspective. In another article, Dr. Hudson also provides important information on breast cancer in women who received chest irradiation for childhood Hodgkin's disease. Finally, we include a feature on the role of family history and "cancer genes" in the occurrence of cancer.

Upcoming study: We are about to begin a new study of long-term health care needs of study participants. We are interested in finding out how you feel about your health care and any problems you may have experienced when going to a doctor. The study will be headed by Dr. Kevin Oeffinger of Children's Medical Center of Dallas. We plan to invite a randomly selected group of study members to participate by completing an eight-page questionnaire. If you are selected you are of course free to choose whether or not you would like to participate. The information you provide is confidential, just like all the other aspects of your participation in the Long-Term Follow-Up Study.

Follow-up questionnaire: Some of you have already received a copy of the follow-up questionnaire that we are sending to all participants. Those of you who have not can expect to receive one in the next few weeks. As always, we appreciate your help in keeping study information up-to-date.

Resources: The Patient Advocate Foundation is a national non-profit organization that offers many types of help to people who have survived life-threatening, chronic or debilitating diseases. Each year the foundation offers a number of college scholarships. For details about scholarships and other services provided by the foundation, you can visit their website:

<http://www.patientadvocate.org>

The foundation's mailing address is:

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Study update: Secondary cancers

Our researchers recently completed an investigation of second cancers among participants in the Long-Term Follow-Up Study. Dr. Joe Neglia and Dr. Deb Friedman, pediatric oncologists at the University of Minnesota and Seattle Children's Hospital, headed the study. The results are presented below.

The occurrence of second cancers (that is, new primary cancers, not relapses or metastases) has been recognized for many years as a possible consequence of cancer treatment. Such secondary cancers are rare compared to the total number of people cured of their cancer, however.

Long-Term Follow-Up Study researchers wanted to find out how often second cancers actually occurred in our study population and what factors are involved in determining

HEALTH HABITS FOR CANCER PREVENTION*

- Don't smoke.
- Exercise regularly, at least three times a week.
- Maintain a healthy body weight.
- Eat four to six fruits and vegetables a day.
- Drink alcohol only in moderation, if at all.
- Don't take illegal drugs or recreational inhalants.
- Avoid exposure to the sun and use sunscreen, particularly on irradiated skin.

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who is at risk. They studied the records of 13,581 study participants and found that 298 of these individuals had developed a second cancer. Of the 298 people who got a second cancer, 16 also developed a third cancer, so that a total of 314 secondary cancers occurred in the entire group. The most common second cancers (excluding basal cell cancers of the skin and benign tumors) were breast cancers (60), thyroid cancers (43), brain tumors (36), and bone cancers (28).

Overall, compared to the general population the risk of secondary cancer was found to be low. However, the risk of getting a second cancer was found to be higher for some

groups of survivors than for others. Study investigators found that several factors increased the risk of getting a second cancer:

- Treatment with radiation therapy
- Female gender (only for breast cancer)
- Young age at diagnosis
- Original diagnosis of Hodgkin's disease or soft tissue sarcoma
- Treatment with high doses of anthracyclines or epipodophyllotoxins. Anthracyclines include the drugs daunorubicin (also known as Daunomycin), doxorubicin (also known as Adriamycin), and idarubicin. Epipodophyllotoxins include VP-16 (also known as etoposide) and VM-26 (also known as teniposide).

People in these groups have an elevated risk even though the overall risk in the entire cohort is low.

This study shows that second cancers after childhood cancer therapy are fairly rare among participants in the Long-Term Follow-Up Study. For most people no special screening or follow-up for second cancers is needed. But it is important for both you and your doctor to know the details of your treatment so you can determine if you are in a group that is at increased risk. If you are, your doctor will recommend the appropriate screening tests for you. It is also important to remember that all survivors, regardless of their risk status, can minimize their chances of getting a second cancer by practicing good health habits.

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Thinking about secondary malignancies

by Melissa Hudson, MD

Learning about the risk of second cancer can be frustrating and anxiety-provoking. After your battle with childhood cancer, the last thing you want to be reminded about is the risk of developing a second cancer during adulthood. In fact, for a variety of reasons, the risk of cancer increases for everyone as they age. Several studies have shown that as childhood cancer survivors become older, they have a slightly higher risk of developing (a second) cancer compared to people their same age in the general population. Things that can contribute to this risk are the person's age during therapy, their specific treatment, and their genetic and family history.

Who is at risk for second cancer?

People who received certain chemotherapy drugs. Some treatments for childhood cancer increase the risk of second cancers. Rarely, people can develop acute myeloid leukemia after treatment. Secondary leukemia usually occurs, if at all, within the first 10 years following treatment of the original cancer. The risk of developing a secondary leukemia is increased for people who were treated with high doses of alkylating agents, epipodophyllotoxins, and anthracycline chemotherapy drugs. The use of these drugs has now been restricted to patients in most danger of relapse. As a result, the risk of developing secondary leukemia has declined dramatically.

People who received radiation therapy, especially at a young age. Radiation therapy given for childhood cancer increases the risk of developing a secondary solid tumor cancer 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 to secondary leukemias, secondary solid tumors most commonly appear 10 or more years after treatment. The risk of developing secondary solid tumors is increased when radiation is delivered at high doses and over large fields to children at a young age. Newer equipment and techniques allow radiation oncologists to treat just the areas involved by cancer and shield normal tissues.

People who have a history of cancer in their 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. To determine if your family history suggests the presence of gene changes that predispose to can-

cer, see the article entitled "Cancer genes and your family" featured on page four of this newsletter.

What if you are in a high-risk group?

You can find out if you are in a high-risk group to develop a second cancer by going over your cancer treatment and family history with your doctor or a cancer specialist. In some cases, early or more frequent screening may be recommended to increase the likelihood that second cancers are detected early, when they are most effectively treated. An example of a high-risk group for which special screening is recommended is people, especially girls, who were treated with chest radiation therapy (see the article entitled "Breast Cancer following childhood Hodgkin's disease" on page 4).

Finally, if you were treated for childhood cancer it is crucial for you to practice good health habits. Some of the health behaviors associated with cancer risk are well known, for example, cigarette smoking and lung cancer, or sun tanning and skin cancer. The risk of a secondary lung cancer or skin cancer may be increased for people whose treatment included radiation to these tissues and who choose to practice the high-risk behavior. People who were treated for childhood cancer should review their health habits and practice behaviors that will help keep their risk of second cancers to a minimum. *Dr. Hudson is the director of the After Completion of Therapy (ACT) Clinic at St. Jude Children's Research Hospital in Memphis, Tennessee.*

FOR FURTHER READING . . .

Breast cancer and other second neoplasms after childhood Hodgkin's disease. by: S Bhatia et al. In: *The New England Journal of Medicine*, 1996: Volume 334, pages 745-51.

Bone sarcomas linked to radiotherapy and chemotherapy in children. by: MA Tucker et al. In: *The New England Journal of Medicine*, 1987: Volume 340, pages 351-57.

Second cancers following pediatric Hodgkin's disease. by: SL Wolden et al. In: *The Journal of Clinical Oncology*, 1998: Volume 16, pages 536-44.

Second neoplasms after acute lymphoblastic leukemia in childhood. by: JP Neglia et al. In: *The New England Journal of Medicine*, 1991: Volume 325, pages 1330-36.

Second malignant neoplasms following treatment for Wilms tumor. by: NE Breslow et al. In: *The Journal of Clinical Oncology*, 1995: Volume 13, pages 1851-59.

Breast cancer following childhood Hodgkin's disease

by Melissa Hudson, MD

Several studies have shown that women treated with radiation to the chest for childhood Hodgkin's disease have an increased risk of developing breast cancer as they get older. Researchers are studying this problem to better understand the risk factors and find ways to prevent secondary breast cancer.

The risk of secondary breast cancer is related to dose of radiation and may be related to age at treatment and family history. Patients treated with the higher doses of radiation have the highest risk. Some studies show that girls irradiated during puberty are also at increased risk. Women in families known to carry gene changes (mutations) that predispose to breast cancer also appear to have an increased risk of developing breast cancer after radiation therapy for Hodgkin's disease. However, information about this is limited because no studies have been done in large groups of childhood cancer survivors.

The risk of secondary breast cancer becomes elevated five to nine years following radiation therapy and continues to rise after 10 years. This means that the age at diagnosis of a secondary breast cancer in a childhood Hodgkin's survivor is much younger (usually 30 to 40 years old) than in women who develop primary breast cancer (usually age 50 or older).

Hodgkin's survivors treated with radiation therapy should perform monthly breast self-examination to increase awareness about breast changes during the menstrual cycle and to monitor for changes suspicious for cancer. They should have breast exams by their doctors twice a year, and a baseline mammogram five to 10 years after radiation. At St. Jude, where I practice, we do the baseline mammogram at age 25 years. The frequency of follow-up mammograms should be decided by your doctor, based on physical exam findings and family history. Starting at 40 years of age, a screening mammogram should be done every year.

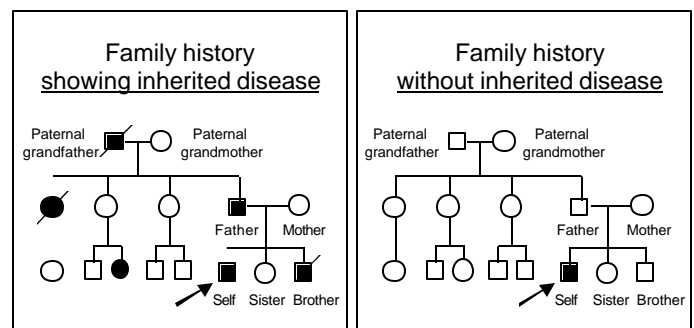
Cancer genes and your family

The cause of most cancers, especially childhood cancers, is not known. Researchers suspect that cancers are caused by a combination of inherited factors and exposures to cancer promoting agents in the environment. You may have asked yourself "Does cancer run in my family?" Scientific studies have focused on this question of inheritance for many years. All of the answers are not available yet but we do know more than we did even a few years ago. Here are

some important points for you to know:

- ❑ Cancer is due to changes that occur at the level of our genes, in specific cells or tissues, allowing cells to grow out of control.
- ❑ Most cases of cancer are not inherited (passed from one generation to the next).
- ❑ There are some types of cancer that do "run in families". The family medical history can give clues to these types of cancer. These clues include:
 - Cancer occurring at a younger age than expected,
 - Rare types of cancer,
 - Many family members in more than one generation with the same type of cancer or specific combinations of cancer,
 - Cancer in both sides of paired organs (for example, both eyes, breasts, kidneys, etc.),
 - Family members with more than one kind of cancer.
- ❑ In most cases the risk of cancer in a brother or sister of a person with cancer is about 1 in 300.
- ❑ Except in families with identified cancer genes, the risk of cancer in the children of a person with cancer is similar to the risk for children of individuals who have not had cancer treatment.

Participants in the Long-Term Follow-Up study did a family medical history as part of the first questionnaire. In certain cases we may need to ask you to clarify information you gave us. If we call you for a clarification it does not mean that your family is at increased risk of cancer. In the future we will be asking study participants to update their family history information. If you have questions or think that cancer may "run in your family" you should talk to your doctor. A review of your family medical history will tell whether genetic counseling or testing is needed.



Using information provided by family members, researchers create pictures like these, called pedigrees, to help show if a certain disease runs in a family. In each of the above diagrams, the arrow points to the person who is giving the information. Circles stand for females and squares stand for males. A diagonal slash through a shape means that person has died. A shaded shape means that person has the disease we are studying. The people near the top are those of the oldest generation, while those at the bottom are the youngest. (Thanks to study investigator Nina Kadan-Lottick, MD)