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- Texas Children's Hospital
- University of California at San Francisco
- Seattle Children's Hospital & Medical Center
- Toronto Hospital for Sick Children
- St. Jude Children's Research Hospital
- Children's Hospital of Columbus
- Roswell Park Cancer Institute
- Mayo Clinic
- Children's Hospitals and Clinics of Minnesota
- Children's Hospital of Philadelphia
- St. Louis Children's Hospital
- Children's Hospital of Los Angeles
- UCLA Mattel Children's Hospital
- Miller Children's Hospital
- Children's Hospital of Orange County
- Riley Hospital for Children-Indiana University
- UAB/The Children's Hospital of Alabama
- University of Michigan-Mott Children's Hospital
- Children's Medical Center of Dallas

From the editor

It's always nice to see summer come back again (especially here in Minnesota.) We can put away the big coats and look forward to more time outdoors. It is a great time to look at our own health and take stock of our habits and experiences that could impact our health in the future. This issue of the newsletter reports on two pertinent studies of secondary cancers in LTFU Study participants. The details follow, but we all should be reminded of the need for proper diet, exercise, regular check-ups, and the avoidance of excess sun as part of our health care plan. Summer is a good time to begin these healthy habits (if you're not doing them already.) Preventive medicine begins with each of us.

Update on Coordinating Center transition. In the last edition of the newsletter we reported that the LTFU Study Coordinating Center will be moving to St. Jude Children's Research Hospital in Memphis where Dr. Les Robison, the Study's principal investigator, is now located. The move process is proceeding about as expected. It is scheduled to be complete by the end of 2006. As we mentioned last time, the University of Minnesota will remain active in the Study, and most participants will not see many changes in their contacts with us.

 **"A Lion in the House."** We would like to alert our readers to an upcoming television series that will be broadcast on U.S. public television June 21-22. The series is called "A Lion in the House." It follows the stories of five young people with cancer and their families and caregivers over a six-year period. This series addresses issues involved with cancer survivorship, including the problems many survivors have with health effects occurring later in life. In conjunction with the broadcast, many public television stations are holding a community engagement campaign, with additional local programming and forums open to the public. "A Lion in the House" will be aired at 9 pm, Eastern time. Your local station can provide information about broadcast and re-broadcast times in your area, as well as about local campaign events.

An overview of the series and the community campaign is available online at the following website:

www.itvs.org/outreach/lioninthehouse/

With our thanks. Enclosed with this newsletter is a listing of the LTFU Study's published research findings to date with information about how you can locate any of the publications you might want to read. Every publication on the list was made possible by the generosity of study participants in sharing important information about your lives and experiences over the past decade. We thank you!

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Study update: Risk of specific adult cancers

Whether we like it or not, the risk of cancer increases for all of us as we get older. Previous reports from the LTFU Study have shown that some survivors of childhood cancer and similar illnesses have a higher risk of developing a second cancer compared to other people their age. This may include a higher overall risk for any type of cancer, or a higher risk of a specific type of cancer, such as breast cancer or thyroid cancer. The risk of developing cancer as an adult is related to many causes including inherited factors (genes), environmental exposures, and risky health behaviors like smoking or sun-tanning. Beyond these factors that affect everyone, people who had a childhood illness like cancer may have an increased risk of getting certain cancers as adults because of the treatments they received to cure their disease. Two recent reports from the LTFU Study focused on the occurrence of several adult-type cancers in people treated for cancer and similar childhood illnesses.

Thyroid cancers. The first study, led by Dr. Alice Sigurdson, looked at the occurrence of thyroid cancers among LTFU Study participants. Thyroid cancer is a complication that occurs rarely after treatment for a childhood illness like cancer and most thyroid cancers can be cured. The risk of developing a thyroid cancer is raised for people who received therapeutic radiation to treat their childhood illness. The research team wanted to find out if the risk was greater for those who received higher doses of radiation exposure. That is, did the risk increase as the dose increased? This is a common pattern and a good sign that an exposure (in this case, radiation) is helping to cause a disease (in this case, thyroid cancer). The evidence of such a relationship between radiation and thyroid cancer risk was unclear before the researchers did this study. Surprisingly, they found that risk did indeed go up as radiation dose increased, but only to a point. For people who received high radiation doses (30 Gy or more) the risk of developing a thyroid tumor was less than expected. The researchers theorized that an explanation for this finding might be that cells which might have turned cancerous were instead destroyed by the higher doses of radiation.

The team found that, as expected, people who had childhood Hodgkin's disease were at greater risk than those who had radiation treatment for other types of childhood cancers. Part of this extra risk is explained by the fact that Hodgkin's survivors usually receive close follow-up care and screening for thyroid problems. This study also confirmed that thyroid cancers tend to develop 10 or more years after treatment for a person's original cancer. In their report, the researchers emphasized the importance of lifelong follow-up, including yearly exams of the neck and thyroid gland, for everyone who received head and neck or chest radiation to treat their childhood illness.

The study is important because, thanks to medical records and questionnaire data provided by LTFU Study participants, it was able to show, conclusively and in detail, the role of radiation exposure in the development of thyroid cancers that occur after childhood illness. The report of this study was recently published in *The Lancet*.

Adult-type carcinomas. The second study, led by Dr. Mylène Bassal and Dr. Nina Kadan-Lottick, looked at how often study participants reported being diagnosed with an adult-type carcinoma involving tissues of the head and neck, lungs, stomach and bowel, kidneys and bladder, or reproductive organs. Fortunately, the overall risk of a LTFU Study participant developing one of these adult-type carcinomas was very low – less than half of one percent at 20 years after treatment. But these cancers did occur four times more frequently in LTFU Study participants than in people who had not been treated for a serious childhood illness like cancer. The risk was higher for those who had received radiation and/or platinum or alkylating-agent chemotherapy. Also, people with certain types of childhood cancer appear to have an increased risk for specific adult-type carcinomas. For example, renal cell carcinoma (a kidney cancer) occurred more commonly in participants who had been treated for neuroblastoma. A carcinoma involving the salivary glands (mucoepidermoid carcinoma) more frequently developed in individuals treated with radiation therapy for a childhood sarcoma (a cancer that grows in connective or supportive tissue, such as bone, cartilage or muscle). The diagnosis of carcinoma was also made at a much younger age than when these cancers usually occur. Almost all cases were younger than 40 years old. Most adult-type carcinomas occur between the ages of 40 and 70 years.

Take control: Practice healthy habits

- **Don't smoke or use tobacco – quit if you do!**
- **Get regular exercise**
 - at least 3 times a week for 30 minutes
- **Maintain a healthy body weight**
 - talk to your doctor if you need help losing weight
- **Eat at least 4 to 6 fruits and vegetables every day**
- **If you drink alcohol, drink in moderation**
- **Get regular health screenings**
 - yearly checkup
 - monthly breast self-exam
 - routine pap smear

This study has been published in the *Journal of Clinical Oncology*.

Comment from Dr. Melissa Hudson

These types of studies help us understand who is at risk of developing serious health problems after being treated for a childhood illness like cancer. They also help us learn how great is the risk, and how and when health problems are likely to develop. The information we get from these studies helps us to inform survivors and their doctors about possible treatment-related health problems. LTFU Study results also provide important feedback to doctors and scientists who are developing and testing new treatments for childhood cancer.



Dr. Hudson

Certain facts that we have learned from these two recent studies should be emphasized:

Survivors who were treated with radiation to the head and neck or chest are at increased risk of developing thyroid cancers. While most thyroid cancers can be cured, early detection is important so yearly medical exams of the neck and the thyroid gland are essential. It is also important to know the details of your treatment history. To minimize your risk, 1) review your health history and treatment to determine if you are in a high-risk group, 2) discuss this risk with your primary care physician, 3) get regular check-ups to increase the chance of early detection, and 4) remember that if you were treated with radiation to your head and neck or chest you must receive lifelong follow-up because these cancers tend to occur many years after a person's original illness.

Adult-type carcinomas involving the head and neck, lungs, stomach and bowel, kidneys and bladder, or reproductive organs occur infrequently after treatment for serious childhood illnesses like cancer. However, individuals who had certain specific types of childhood cancer and those who had certain treatments are at increased risk. Adult-type carcinomas that develop after childhood cancer typically occur long before the usual age these conditions occur in the general population. Again, you should 1) review your history and treatment to determine if you are in a high-risk group, 2) discuss your risk with your primary care physician, remembering that he or she may not be aware of the risk of early occurrence of these cancers that some survivors face, 3) get regular check-ups, and 4) promptly report warning signs of adult cancer to your doctor. Health habits have been shown to play a big role in the risk of many of these adult-type carcinomas, so practicing healthy behaviors is especially important for childhood cancer survivors.

LTFU study toll-free phone number:
1-800-775-2167

Know the 7 warning signs of adult cancer

1. Unusual bleeding or discharge
2. A sore that does not heal
3. Change in bowel or bladder habits
4. Thickening/lump in breast or elsewhere
5. Nagging cough/hoarseness that doesn't go away
6. Obvious change in a wart or mole
7. Indigestion or difficulty in swallowing

Finding a doctor who understands

People who were treated for a serious childhood illness like cancer often report that it can be hard to find a physician who is both *familiar* with their unique health issues and *comfortable* managing their care. Because childhood cancer and similar illnesses are uncommon, the chance of finding a doctor who has a lot of experience in this area is rare. Some doctors may have one or two adults in their practice who were treated for childhood cancer, but most will have none. On its website, the Association of Cancer Online Resources (ACOR) has published a listing of long-term follow-up clinics to help survivors connect with healthcare providers who are knowledgeable about their unique healthcare needs. To be included on this list, a center must have a dedicated time and place for a survivor clinic that meets at least twice a month. The staff of the clinic will usually include a doctor and/or a nurse coordinator with experience in late effects after treatment for childhood cancer. The follow-up clinics typically offer services such as screening for delayed health problems that can result from a person's prior treatment, referrals to subspecialty care as needed, and wellness education. The list of clinics and their contact information can be found at this link:

www.acor.org/ped-onc/treatment/surclinics.html

So far, over 30 clinics, providing services in over 20 states, are listed. Some clinics only provide care to child or teen survivors, while others also provide care to adult survivors. Other centers see only adults who have been treated for childhood cancer. Finally, some clinics see only survivors who received their childhood cancer treatment at their centers. The ACOR clinic list may help you identify a late effects specialist in your area who can work with your primary care doctor to outline a follow-up plan. If you attend one of the clinics, it is important to provide feedback to ACOR about your experience. The ACOR site includes a link to a brief survey that asks you about the services provided by the clinic and how well the clinic staff served you.

If you're not eligible for a clinic on the ACOR list ...

Because of distance or insurance issues, some survivors will not be able to arrange an appointment at one of the follow-up clinics. For these individuals, the best option is to ask the doctor who treated your childhood cancer to write a letter summarizing your diagnosis and treatment, likely health risks associated with your diagnosis and treatment, and recommended screening tests. If you cannot find a physician who is available or willing to do this, you should request copies of your treatment records so you will at least have information about your diagnosis and treatment that can be used by your current doctor to plan your care.



"The medical staff in long-term follow-up clinics are familiar with potential late complications of treatment such as treatment-related malignancies and cardiovascular disease, which would not normally occur in individuals as young as many of our survivors are." —Dr. Daniel Green

Using the COG screening guidelines. The Children's Oncology Group's long-term follow-up screening guidelines for survivors of childhood, adolescent and young adult cancers are an important tool to help survivors and healthcare providers learn about the health risks survivors face, based on their specific diagnosis and treatment (see the example below). Please inform your primary care doctor about this important resource. You will find the COG screening guidelines at the following website:

www.survivorshipguidelines.org

Follow-up clinic to the rescue

When she was diagnosed with stomach cancer, LTFU Study participant **Carol Schultz** wasn't experiencing any symptoms except for fatigue. Her primary care doctor told Carol she was just tired because she was getting older. But Carol, who had survived Wilms tumor (a cancer of the kidney) as a child,

knew her fatigue was more than just a sign of aging. Carol had been treated for her childhood cancer at Roswell Park Cancer Institute in Buffalo, New York. Fortunately, Roswell Park has a long-term follow-up

clinic. Carol made an appointment to see clinic director and LTFU Study investigator, Dr. Dan Green. Because she had received radiotherapy as a child for her kidney tumor, Dr. Green wanted to rule out any problems in her abdominal area. Tests revealed the cause of Carol's fatigue: a malignant tumor in her stomach. The tumor was caught early, at Stage I, and was successfully removed along with two-thirds of Carol's stomach. "Just because it [childhood cancer] was 29 years ago," Carol reflects, "doesn't mean it's behind you."

Carol's participation in the LTFU Study helped her be aware that she might be at risk for health problems occurring later in life. She says, "In the past I've thought of quitting the study—I didn't want to fill out more of those forms!—but it is so important to stay with the program. It has saved my life."

Editor's note. Thank you, Carol. We are very glad you were able to connect with a long-term follow-up clinic!

Using the COG screening guidelines

As an example of using the COG guidelines for long-term follow-up screening, let's assume that a woman was diagnosed in 1988 at age 15 with Hodgkin's disease involving lymph nodes in her neck and chest. The table below shows the possible health risks associated with her treatment history. Screening recommendations for all of these treatments can be found in the CureSearch Children's Oncology Group Long-Term Follow-Up Guidelines at: <http://www.survivorshipguidelines.org>.

TREATMENT HISTORY	LONG-TERM HEALTH RISKS
Staging surgery with spleen removal (splenectomy)	Removal of the spleen results in a lifelong risk of a serious blood infection with certain bacteria that are handled by the spleen. People who have had their spleens removed are advised to seek prompt medical attention if they develop a fever of 101° F or more.
ABVD chemotherapy - six months Adriamycin Bleomycin Vinblastine Dacarbazine	People who had ABVD chemotherapy are at risk of heart problems related to the Adriamycin and for lung problems related to the bleomycin they received. The risk is related to the dose of these medicines. Dose can be estimated by the number of months of treatment. Most people do not have long-term problems after receiving vinblastine and dacarbazine, the other drugs in this combination.
Radiation to lymph nodes in the neck and chest - eight weeks	Radiation to the lymph nodes in the neck and chest may have long-term effects on the salivary glands, thyroid gland, heart, and lungs. The risk is related to the dose of radiation, which can be estimated by the number of days of treatment. Radiation of any tissue also increases the risk of developing a second (different) cancer. Girls who had radiation to the chest for a childhood cancer are at increased risk of developing breast cancer.
Blood transfusion in 1988	Before 1992, blood banks did not have a reliable way to test if blood donors were infected with hepatitis C, so people who received a transfusion before that time are at risk of developing chronic hepatitis C infection. This increases the risk of liver problems, including liver cancer.

For more than a decade, LTFU Study participants have generously provided us with important information about their experience of surviving childhood or adolescent cancer, leukemia, tumor, and similar illnesses. As a result, the Study has produced a remarkable number of important research papers. These papers have been published in some of the best medical journals. Occasionally, they have made national, and even international, headlines. For your reference, we provide below a complete list of the findings the LTFU Study has published to date. Thank you very much for your continued participation and help!

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