

LTFU

Long-Term Follow-Up Study

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UNIVERSITY OF MINNESOTA

Spring 2007

Memphis, Tennessee

We hope you're well and enjoying the warmer spring weather. After a smooth transition period, activities of the LTFU Study are now being coordinated from Memphis. For details on the progress of Study projects, see the box below.

In this issue of the newsletter, we look at treatment effects on your sexual and reproductive health. We chose this topic because adults who had serious illnesses during childhood may face midlife changes earlier than others. As a result of treatments used to cure their diseases, some girls stop having menstrual periods soon after the end of treatment. Others may go through early menopause years or even decades later.

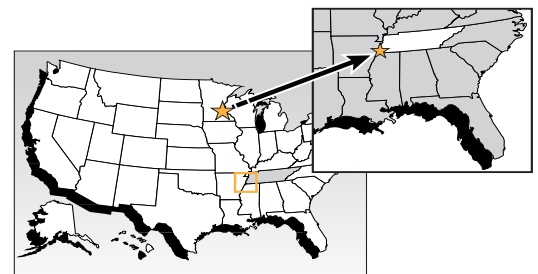
Other changes in women *and men* are not so easy to see. These changes result from the reduced levels of sex hormones that go along with the shift to midlife. Their effect on our minds and bodies is complex and inter-related. Examples include decreased sex drive, reduced bone mineral density and muscle mass, and greater risk of disease, especially heart and blood vessel disease. In the study update section, we report on the results of three recent LTFU studies that looked at the fertility and pregnancies of Study participants. Dr. Hudson's comments (page 3) explain how the effects on reproductive and sexual function extend to your overall health.

The study results reported here are important for several reasons. Knowing about the experiences of others can help couples make decisions about when to plan a pregnancy or when to consider other options for starting a family. Awareness of risk may prompt others to take steps to protect their health. This issue's survivor story shows a few simple ways one person did just that. To find out how she stays on her toes managing her life, an active family, and her own health, see the story on page 4.

—Margaret Carbaugh, editor

Members of your new coordination staff are already busy working on Study projects such as the Follow-Up 2007 survey, which will be mailed soon. For the first time, you will be able to complete the questionnaire on the Web. See the cover letter to your questionnaire for more details.

We've Moved
to Memphis,
Tennessee.



Note the change in the web address since the move of our coordinating center to St. Jude (www.stjude.org/ltfu). Our telephone number is the same (1.800.775-2167). We welcome your feedback on this LTFU Study Update.

Safeguarding Fertility

Few issues are as personal or important as those that affect our sexual health and the ability to become pregnant and to have a healthy pregnancy. Among adults who received treatment for a serious illness as a child, these issues take on added weight.

In some cases, the treatment used to cure their illness may have affected their sex organs and ability to have children. Some boys may have needed sex hormones to reach the height, body mass, and bone density of other boys their age. And, girls may have needed hormones to start having menstrual periods. Some women may quit ovulating during treatment or shortly after, while others may go through menopause early.

In LTFU results published this year, there is good news for Study participants. The offspring of those who are still able to have children generally fare well. And, those facing midlife changes sooner than expected can take steps to prevent or lessen the unwanted and annoying side effects they may encounter.

See the summaries below for more details.

Reproductive Health ... Early Menopause

In a special study of women's health, LTFU researchers looked at the *risk of premature menopause* among those who continued having menstrual periods for at least 5 years after their cancer diagnosis.

Those who experienced *non-surgical premature menopause* were alike in several ways. They were more likely to have been older at follow-up, to have had Hodgkin lymphoma, and to have received *alkylating agents* or radiation to the pelvic area. Those who received both types of treatment were the most likely to go through menopause at a young age.

"We hope that the results will help Study participants in planning their families and in the timing of future pregnancies," says Charles A. Sklar of Memorial Sloan-Kettering Cancer Center, who led the study. "Those with the highest risk of premature menopause may choose to have children when they're younger and more likely to be fertile."

Women who go through menopause early should take steps to protect themselves from the increased risk of *osteoporosis* and heart disease. For links to helpful web sites, see the box on the bottom of page 4. The study team looked at data of 2,819 LTFU participants and 1,065 siblings. Results were published in the *Journal of the National Cancer Institute* (July 2006).

Reproductive Health ... Ovarian Function

In another study, the same team found that Study participants who quit having menstrual periods within 5 years of treatment (*acute ovarian failure*) had several factors in com



Dr. Charles Sklar

Definition of key terms

Risk — likelihood of being harmed; **Premature menopause** — when a woman stops ovulating and having menstrual periods before the age of 40; **Surgically induced premature menopause** — menopause due to removal of the uterus or one or both ovaries; **Alkylating agent chemotherapy** — a type of chemotherapy that may cause injury to certain body organs, including the ovaries and testes. Examples include cyclophosphamide and procarbazine. **Fertility** — ability to have children; **Ovarian failure**— when the ovaries stop production of eggs or sex hormones; **Osteoporosis** — Silent bone disease caused by a drop in bone mass that makes bones brittle and more likely to break

mon: They were more likely to have been older at diagnosis and to have received radiation to their ovaries. Treatment with certain alkylating agents was also a risk factor.

"Knowing who has increased risk will help in counseling future patients and families before the start of treatment," says Sklar. "And, it will allow us to identify patients most likely to benefit from new techniques to preserve *fertility*." The study team looked at questionnaire responses and medical chart data of more than 3,300 women in the LTFU Study. Results were published in the June 21, 2006, *Journal of Clinical Endocrinology and Metabolism*.

Both studies led by Sklar were funded by the National Institutes of Health.

Check out these sites for information about fertility and family planning:

Fertile Hope	fertilehope.org
Lance Armstrong Foundation	livestrong.org
American Society for Reproductive Medicine	asrm.org
Dave Thomas Foundation for Adoption	davethomasfoundationforadoption.org

Health of Offspring

Another LTFU study team found that the rates of miscarriage were no higher among Study participants or their partners than among siblings. Although babies of Study participants weighed less at birth, their lower weight was probably due to being born preterm. Results were published in the Oct. 18, 2006, issue of the *Journal of the National Cancer Institute*.

Men's Health Questionnaire and 2007 Questionnaire

Men in the LTFU Study will soon be asked to take part in a study of male sexual function. The request will appear in the form of a question on the 2007 questionnaire, which will be mailed soon.

According to Lillian Meacham, MD, of Emory University and the principal investigator, the study will seek to answer questions regarding the hormonal function, fertility, and sexual function of male survivors.

Results will be used to help establish guidelines for follow-up care. The study is funded by the Lance Armstrong Foundation.

Reproductive and Sexual Effects Extend to Overall Health

More and more children with cancer and other serious illnesses are surviving to adulthood. As a result, we've become more aware of the effects of treatment on survivors' sexual and reproductive health. By "reproductive health," we mean the ability of women to bear healthy children. We're also talking about the ability of men to sire healthy children. Now, large groups of survivors are entering midlife. As they do, we've shifted our focus some.



Dr. Melissa Hudson

We are still concerned about issues of childhood, puberty, and young adulthood. Normal growth and development and treatment effects on child-bearing and the health of offspring are still important. But, we're starting to see, and to study, the ways in which effects on the sex organs shape overall health. Many parts of the body play a role in sexual function and having children. But when we refer to "sex organs," we mean the ovaries and testes.

We now know that some cancer treatments can affect the sex organs in ways that harm fertility. The most common are listed in the box to the right. For details about some treatments linked to infertility in women, see the study updates on page 2. In general, it's been easier to study women's reproductive health. As a result, we know more about risk factors for women. It's also very important to learn more about cancer's effect on men's sexual and reproductive health.

Our hope is that your replies to the Men's Health Questionnaire will help us do just that. See the box on page 2 to learn more about this study. What we learn will help us deal with the health concerns of men who had cancer or another serious illness as a child. So, please take part!

What we now know about your sexual and reproductive health is just the tip of the iceberg. Harm to reproductive function may have many effects on overall health we don't yet know about. It's clear that sex hormones are needed for the body to develop during puberty and for sexual function and having children. They also play an important role in bone health, heart and blood vessel health, and overall quality of life.

As we age, the usual fall in levels of sex hormones seems to lead to lower bone mineral density. In turn, lower bone mass may lead to weaker bones that are more prone to fracture.

In the general population, we see these conditions more often in women who have gone through menopause. Of course, these women no longer make the female sex hormone estrogen. Bear in mind that both men and women can have low or below normal levels of sex hormones after cancer treatment. They too are at risk of lower bone mineral density. For them, hormone therapy may help preserve bone strength and prevent fractures.

Hormone therapy also helps treat the annoying side effects often reported by those with low levels of sex hormones. The possible risks and benefits of hormone therapy may vary based on specific cancer treatment and family history. This is why it's important to discuss treatment options with a doctor who knows your health and family history.

Treatments that Affect Ovaries and Testes

- Alkylating agent chemotherapy (such as cyclophosphamide or procarbazine)
- Irradiation of the ovaries, testes, or brain
- Surgery involving the pelvis or reproductive organs

Reproductive Changes that Harm Fertility

- Lower hormone levels (estrogen and testosterone)
- Damaged eggs (oocytes) or sperm
- Reduced number of eggs or sperm
- Scarring of the following:
 - reproductive organs
 - fallopian tubes
 - nerves that control sexual function
 - uterine lining
 - blood vessels of reproductive organs
 - duct system that transports sperm

Possible Benefits of Hormone Therapy

Women (Estrogen)

- Reduces hot flashes
- Reduces vaginal dryness
- Improves mood and concentration
- Preserves bone strength
- Prevents fractures

Men (Testosterone)

- Helps maintain lean muscle mass
- Reduces body fat
- Improves sex drive
- Preserves bone strength
- Prevents fractures

Possible Risks of Hormone Therapy

- Heart and blood vessel disease
- Blood clots
- Strokes
- For women, breast, uterine, and ovarian cancer (if they received chest radiation or have a strong family history of these cancers)

Health Link Handouts Available on Web

The Children's Oncology Group's web site has easy-to-read handouts that give information on reproductive and sexual health issues of men and women who received treatment for cancer during childhood.

These and other topics of interest to adult survivors of cancer, leukemia, and other serious illnesses can be found at www.survivorshipguidelines.org.

Notes from Survivors

Childhood Leukemia Survivor Manages Life, Family, Health

In January of this year, Blair Huddleston Collins of Richmond, Virginia, celebrated her 37th year as a survivor of childhood leukemia by running in her first marathon and helping to raise \$5 million dollars for leukemia research.

Keenly aware of the potential for adult health issues resulting from childhood treatment, Blair understood the importance of a regular health and fitness routine. To help achieve her fitness goals, she had already been working with a personal coach when she decided to train for the marathon. Her commitment to help raise money by running in marathons is just one way she “gives back” to those whose work saved her life more than 30 years ago.

Blair was just 3 years old when doctors diagnosed her disease as ALL (acute lymphoblastic leukemia). After a year of in-patient treatment, Blair received radiation therapy and chemotherapy as an out-patient until the fourth grade. Since then, she has never experienced a relapse (disease recurrence).

Before treatment began, doctors told Blair’s mother that she would be infertile. Unlike some girls who received radiation and chemotherapy at early ages, Blair began having menstrual periods at about the normal age, and without taking hormones. However, her periods were not regular.

After graduation from high school, Blair attended college in a nearby state. Because she had always loved children, she planned to return to the hospital where she received treatment, possibly to work in grief counseling. She also considered work in a hospital-based program for children undergoing treatment for serious illnesses.

After Blair married Jeff Collins in 1996, the couple started thinking about having a family. Because they thought Blair was infertile, they were pleasantly surprised when she became pregnant. They were looking forward to the birth of a healthy son when Blair had a miscarriage in the fifth month of her pregnancy.

Hopeful that she would become pregnant again, Blair spent the next year trying various fertility treatments. The couple even considered in vitro fertilization, a procedure that improves chances of pregnancy in women and men with low numbers of eggs and sperm.

When attempts to harvest an egg were unsuccessful, the doctor concluded that Blair had already gone through premature menopause. Tests also showed that her uterus was completely blocked with scar tissue due to radiation therapy. With no hope



Encouraged by success with Tyler, Blair and Jeff adopted Kaitlyn in 2005.

of becoming pregnant again, Blair and Jeff began considering other options for starting a family.

Soon after the decision to attempt adoption was made, the couple submitted paperwork to become adoptive parents. Within 6 months, they met their son’s birth mother, who knew “they were the ones” during their first interview.

Today, Blair manages the life of an active family who enjoy biking, camping, and hiking, and canoeing. Although the children don’t go kayaking with their parents “yet,” 2-year-old Kaitlyn already has her own backpack for treks into mountains just two hours away from their home.

Staying on top of her own health also keeps Blair on her toes. She has a bone mineral density test once a year and reduces the menopause-related risk of osteoporosis and heart and vessel disease by working out three times a week. She also watches what she eats. Her diet consists of fish and fresh fruits and vegetables, supplemented by vitamins and calcium.

During her 30s, Blair used vitamin therapy and other natural therapies to counter mood swings, short-term memory problems, and hot flashes. After the hysterectomy, her doctor prescribed hormone therapy, but not until she had weighed the risk of breast cancer against the benefits of estrogen. Currently, she is using a natural hormone cream and says, “I feel wonderful and strong and healthy!”

Check out these helpful web sites to find ways to stay healthy after cancer, leukemia, and other serious childhood illnesses.

Use new dietary guidelines to healthy eating.

Keep track of your fitness program with an online exercise diary.

Keep up-to-date on the latest news about health and fitness.

Find out how much you need to eat from each food group.

Learn ways dairy products can help build healthy bones and bodies.

Use online resources to change eating habits and activity levels.

Find out your risk of osteoporosis.

Learn ways to prevent this condition.

eatright.org

justmove.org

acecfitness.org

MyPyramid.gov

nationaldairycouncil.org

aomamericanonthemove.org

nof.org/osteoporosis/Risk_Factor_Questionnaire.pdf