

LTFU

Long-Term Follow-Up Study

www.cancer.umn.edu/ltfu

University of Minnesota
The Denver Children's Hospital
Children's Hospital of Pittsburgh
Children's Hospital at Stanford University
Dana-Farber Cancer Institute
Children's National Medical Center
U.T.M.D. Anderson Cancer Center
Memorial Sloan Kettering Cancer Center
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 Health Care - Minneapolis
Children's Hospital of Philadelphia
St. Louis Children's Hospital
Children's Hospital of Los Angeles
UCLA Medical Center
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

Inside

Meet the Carsons: Billy, Kim, & Alex	2
Study update: pregnancy outcomes	3
Having children after childhood cancer	3
VOLUNTEERS NEEDED!	4

UNIVERSITY OF MINNESOTA

Winter/Spring 2002

From the editor

One of the more difficult decisions people face is the decision to have children. For some people, it is a straightforward choice, but for others it is complicated by personal, medical, or financial considerations. Sometimes, just being able to gather all of the information needed to make an informed decision is difficult. This can be especially true for someone with a complex medical past. Physicians may have told you (or your parents) that it might be difficult for you to have children, or you may wonder if the disease and treatment you had could affect *your* children's health. This issue of our newsletter focuses on fertility, a person's ability to become pregnant or to father a child. Obviously, there is no "one size fits all" approach to this subject, but we hope you will find the information provided here to be a useful starting point. It is important to base your decision-making in this area on the best information you can get.

Our advice to our patients always starts here: Assume - and act like - you could become pregnant unless you are absolutely sure you cannot. Even though some cancer treatments can increase the risk of infertility (not being able to have children), there are many, many people who have had children after cancer therapy. If you are involved in an intimate relationship with someone, believing that your previous therapy will make pregnancy impossible may not be a good choice.

On the other hand, if you are hoping to start a family, you will find encouraging news here about the pregnancy experiences of our study participants. For some, the information in this issue may not be immediately relevant today, but we hope it can give you at least a start on unraveling a complicated yet important subject.

2002 questionnaire. It has been almost eight years since we mailed out the first study questionnaires! Thanks to you we've learned a great deal about the health effects of treatment for childhood cancer and similar illnesses. Now we are working on a questionnaire that will be quite different from those you have seen in the past. The focus of this new questionnaire will be on your life experiences. We hope you will find it interesting. Please watch for it late this summer.

SPECIAL NOTE: On the back page of this newsletter you will find information about an important new effort to collect blood specimens for research on the genetic aspects of treatment for cancer and similar illnesses. Please take a moment to read about this project. We hope you will consider volunteering to take part. This research is crucial to gaining an understanding of how cancers are caused and how genetic factors may be passed on in families.

Meet the Carson Family: Billy, Kim, and Alex

Billy Carson of Saltillo, Mississippi developed leukemia when he was nine years old. Billy is a participant in the Long-Term Follow-Up Study. He was successfully treated at St. Jude Children's Research Hospital in Memphis, Tennessee. Billy completed therapy in 1982 at age 12. That was years before he started thinking about having children of his own. But after he got married he and his wife Kim had trouble starting a family. Both Kim and Billy were tested to find out if they were able to have children. Kim's tests showed that she was fertile but Billy's tests revealed he had a sperm count of zero. A second sperm count confirmed the results.

Billy had not thought his cancer treatment would affect his ability to have children. Like many people treated for childhood cancer, leukemia or a similar illness, he found out that his disease and treatment would have lasting effects on his life.

Exploring fertility options

Billy and Kim decided to look into assisted reproduction techniques. They went to a fertility clinic in Birmingham, Alabama. The doctors there were able to locate and retrieve a few sperm from Billy.

Billy and Kim hoped they would be able to use the recovered sperm for *in vitro* fertilization of one of Kim's eggs. In this procedure the egg cell and sperm are brought together in a laboratory dish. The fertilized egg is then placed in the mother's uterus to complete the pregnancy. *In vitro* fertilization is very expensive. The Carsons would need to pay \$10,000 and there was no guarantee that the pregnancy would be successful. In addition, Billy's tests had revealed that he had a genetic trait that greatly increased the chances of a miscarriage. The chance of passing on this genetic problem to his children was also high.

Fortunately, there were other options available to the Carsons. They thought about adopting a child. But first, they decided, they would try artificial insemination using an anonymous sperm donor. This procedure is much less expensive than *in vitro* fertilization. Their chances of success were also greater.



Success

Billy describes the five years the couple spent trying to conceive a child as a rollercoaster ride. "When you try and are unsuccessful, it's almost like a death," he says. Finally, after three attempts they got the news they were hoping for. Kim was pregnant. Their son Alex was born January 2, 2001. He is now a year old, walking, and trying out his first words.

Insurance issues

The effects of Billy's cancer treatment weren't the only obstacles in the Carsons' way as they tried to start their family. Getting insurance coverage for assisted reproduction was also a major hurdle. The procedures are very expensive. Many insurance companies don't consider them to be medically necessary, even in cases like Billy's where infertility is a direct result of cancer and treatment.

Billy reasoned that if other aspects of reproduction, like pregnancy and vasectomy, are covered by insurance, fertility treatments should be covered, as well. He submitted and re-submitted his insurance claims, and got supporting documentation from his doctors. He succeeded in getting his insurance company to pay some of the bills, but not all. At one point, the Carsons considered going to court. But they decided the emotional cost of a trial would be too great. Billy says his experience was "like playing a game of tennis. If they reject your claim and you don't do anything then it stops."

The Carsons' experience demonstrates the importance of persistence in dealing with insurance issues. Repeated efforts can lead to success. But Billy wishes there was more support available to people with infertility. "There are a lot of people out there that have the problem," he observes, and few resources are available to them. His home state of Mississippi has no advocacy group. "You're kind of standing alone," he says. He notes that one step people who are denied coverage can take is to appeal to the insurance commissioner in their state.

Future plans

Billy and Kim had to overcome many obstacles on the way to giving birth to Alex. At great cost they learned what works and what doesn't work for them. Pursuing assisted reproduction is not easy and not the only course open to infertile couples. Some may choose to adopt a child. Others may choose to remain childless. It is a very personal decision for each couple. In spite of the difficulties, however, the Carsons have no doubt that they

made the right choice for their family. They are thrilled to be parents and they are planning, some day soon, to have another baby.

Note: *Billy has expressed interest in sharing his experiences directly with our study participants. If you would like to contact him, please call the toll-free study line - 1-800-775-2167 - and we will help to arrange it.*

Study update: Pregnancy

A team of researchers recently completed a study of the pregnancy information provided by our study participants. Dr. Daniel Green of Roswell Park Cancer Center in Buffalo, New York led the study. The researchers wanted to find out if the chemotherapy or radiation treatment study members received as children or adolescents had an effect on their pregnancies. They analyzed the rates of pregnancy loss and the numbers of live births reported by participants. They also looked at birth weights. They reported on the information from female participants and male participants separately.

Females: The investigators found that 1915 female study members had ever been pregnant. They had a total of 4029 pregnancies.

The investigators did not find that most chemotherapy treatments led to pregnancy problems. However, they did find that women who had received radiation to the pelvis were more likely than expected to have low birthweight babies. Babies who weigh less than 2500 grams are considered to be low birthweight. 2500 grams is about 5 ½ pounds. This finding is important because low birthweight can be associated with health problems later in life.

Males: 1227 males reported getting a partner pregnant. The total number of pregnancies they fathered was 2323. For the most part the researchers did not find any problems with the pregnancies fathered by our study participants. However, they did discover two things that will require more study.

First, the partners of men who had been treated with the higher doses of chemotherapy drug procarbazine had more miscarriages than the partners of the men who had received the lowest doses of this drug. Second, our male participants and their partners had fewer boy babies than expected, compared to their siblings.

The results from this study are encouraging. They provide good evidence that the majority of people treated for cancer or a similar illness in childhood or adolescence can have healthy pregnancies. The large number of participants in our study make these findings more reliable than previous studies with smaller numbers. We will be following up on these findings as we gain additional information.

Having children after childhood cancer

by Dr. Melissa Hudson

You may be wondering if the treatment you received for your childhood cancer or similar illness had any effect on your ability to have children. Or you may have been told you are not able to have children because of the therapy you received. Some therapies can cause permanent infertility. But not all therapies affect sperm or egg production permanently. They may only cause a temporary period of infertility. This usually begins during therapy and may last for a year or so after treatment is complete. (If you are infertile, it is also possible that your infertility might have other causes that are not related to your treatment. Approximately 15 percent of all couples are unable to have children.) *However, people treated for cancer or other serious illnesses in childhood or adolescence should not automatically assume they are unable to have children.*

How do I know if I am at risk to be infertile?

Surgery to remove both testes, both ovaries, or the uterus, will result in infertility.

Other treatments known to have an effect on fertility are:

- Radiation of testes, ovaries, pelvis, abdomen or brain;
- Chemotherapy drugs called alkylating agents; these include cyclophosphamide, ifosfamide, nitrogen mustard, and procarbazine.

The risk of infertility is related to the total doses of radiation to critical organs or chemotherapy that you received. The higher the dose of radiation or chemotherapy, the more likely is the risk of permanent infertility. Lower doses often only temporarily affect a person's ability to have children. The risk of infertility may also be higher if radiation is combined with alkylating agent chemotherapy. But there are no hard and fast rules. Sometimes, cancer patients who were thought to be permanently infertile have become pregnant or have fathered a child years after treatment.

How can I tell if I am infertile?

Our bodies make hormones during puberty that help us mature sexually and make it possible for us to have children. Some types of treatment stop the production of these hormones. If you had to take hormones in order to go through puberty you are likely to be infertile.

In girls, the brain and the ovaries make hormones that are needed for egg development and for preparation of the uterus for pregnancy and regular menstrual periods. If a woman

who is *not* on hormones or birth control pills has regular periods, she is likely to be able to become pregnant. If a woman only has periods while taking hormones or birth control pills, she is likely to be infertile. Most women who have stopped having periods are infertile.

In boys, the brain and the testes make hormones that are needed for sexual functioning and sperm development. The most important male hormone is testosterone. The testes also produce sperm. The sperm-producing cells are more sensitive to the effects of cancer therapy than the hormone-producing cells, so it is possible for sperm production to be damaged when hormone production is still normal. Men who have low sperm counts and normal testosterone levels do not have symptoms. Men with low testosterone levels may show symptoms like reduced sex drive and potency. Both these problems can make it difficult for a man to father a child.

What is involved in fertility testing?

For men, the most accurate way to test fertility is to do a semen analysis. A urologist, gynecologist, or endocrinologist can do this test. Along with the semen analysis, they will also check levels of testosterone and other brain hormones that control sperm production.

For women, a menstrual history is taken. A blood test is done to check the level of estradiol, the main female hormone, and other brain hormones that control ovulation. An x-ray of the fallopian tubes may also be taken if other tests are normal.

If I am infertile, what are my options?

You may decide to consult a fertility specialist about assisted reproduction. The simplest technique involves placing the husband's or donor's sperm into the woman's uterus at the time of ovulation. Another common technique is *in vitro* fertilization. This is a procedure in which a donor egg or sperm is combined in a laboratory dish with the sperm or egg from the infertile couple. The fertilized egg (embryo) is then placed directly in the woman's uterus. Assisted reproductive technologies are expensive. And they are not always successful. Some couples decide to adopt a child instead of trying infertility treatments. Others decide to adopt after infertility treatments have failed. If you want to adopt a child, a doctor's letter documenting your cancer-free status and long-term prognosis can help speed the process. Finally, some infertile couples decide that not having children is best for them. It is important to remember that the choice to live childfree involves grieving for the loss of reproductive function.

Are fertility testing and treatments usually covered by insurance?

Insurance coverage of fertility testing and treatments varies

widely by policy. If you are persistent you may be able to get coverage for some procedures. A letter from your doctor sometimes helps. The letter should explain that the infertility is a medical complication of cancer treatment and not a pre-existing condition. Also, if you are denied coverage, you may be able to appeal to your state's insurance commissioner. Our study website (www.cancer.umn.edu/ltfu) has links to online resources that provide information about adoption, fertility, and insurance coverage for assisted reproduction.

Volunteers needed!

Study participants have been very generous in providing information for the Long-Term Follow-Up Study. With your help we are gaining new knowledge about childhood cancer and similar illnesses and about the effects of treatment of these diseases. This knowledge will have an impact on the way children and young adults are treated in the future.

To learn more about these serious diseases we need to add to the information you have provided on our study questionnaires. We are starting a new project to collect blood specimens for research. We will use these specimens to try to discover how cancers grow, why cancer responds to some treatments but not others, and what causes cancer cells to become different from non-cancer cells in healthy tissue. We will also use them to increase our understanding of the genetic aspects of cancer and similar illnesses.

There are two ways in which you can help. First, you can allow us to collect a blood sample from you. This would be done by a trained technician who would come to your home, or other place you choose, to draw the blood. You would not have to go to a doctor's office or hospital. Second, you can allow us to collect blood samples, in a similar manner, from you, your child, and your partner who is the parent of your child. These blood samples will help us understand more about the genetic effects of therapy for cancer and similar diseases. As always, participation in this aspect of Long-Term Follow-Up Study is voluntary and confidential. Any specimens you provide will be used only for research. They will not be sold. The information obtained will not be identified with you in any publication.

We urgently need volunteers for this part of the study. If you would like to be a part of this project, please email us at ccss@epi.umn.edu or call the toll-free study line: 1-800-775-2167.

Thank you for your continuing participation in the Long-Term Follow-Up Study!