

A BRIEF UPDATE

From the Long-Term Follow-Up Study

February 2014

<http://ltfu.stjude.org>

Topic: FERTILITY

Why we studied fertility:

Some treatments in childhood, including radiation and some types of chemotherapy, can cause people to be unable to have children.

Who we studied:

Long-Term Follow-Up Study participants between the ages of 15 and 44:

- 7,516 men (6,224 survivors and 1,292 siblings)
- 6,590 women (5,149 survivors and 1,441 siblings)

What we studied:

Participants' ability to get pregnant or to father a pregnancy, at least 5 years after being diagnosed with cancer.

We found that . . .

- Overall, female survivors were 20 percent less likely to become pregnant than the members of the female sibling comparison group.
- Overall, male survivors were only about half as likely to father a pregnancy as the males in the sibling comparison group.
- Male survivors who did not have any of the high-risk treatments were just as likely as the siblings to father a pregnancy.
- Radiation treatment to areas of the body that included the testicles in males or the ovaries and uterus in females was associated with a higher risk of infertility.
- Treatment with high total doses of alkylating agent chemotherapy drugs also increased the likelihood of infertility for both male and female survivors.

Also at increased risk of infertility were . . .

Men who:

- Were diagnosed at older ages (15-20) compared to other survivors.
- Were treated with the alkylating agent procarbazine or with high doses of cyclophosphamide (Cytoxan).

Women who:

- Were exposed to radiation dose of more than 30 Gray to the hypothalamic/pituitary area of the brain.
- Were treated with the specific alkylating agents lomustine (CCNU) or cyclophosphamide.

Alkylating agents . . .

. . . are a common type of chemotherapy drugs. They have been associated with damage to the gonads (ovaries and testicles). They are used to treat many different types of diseases, including leukemia, Hodgkin and Non-Hodgkin lymphoma, and solid tumors. They include:

BCNU (Carmustine)	Ifosfamide
Busulfan	Melphalan
CCNU (Lomustine)	Mechlorethamine
Chlorambucil	(Nitrogen Mustard)
Cyclophosphamide (Cytoxan)	Procarbazine
	Thiotepa

In summary:

- Treatment in childhood or adolescence for cancer or a similar serious illness sometimes leads to decreased fertility for both men and women. Men are at greater risk than women of being unable to have children.
- The results of this study may be used to counsel future patients about fertility problems that are linked to cancer treatment.

THANK YOU for your continuing participation in the LTFU Study. Watch for the new follow-up survey, which will be sent to you in the coming year.

References

Green DM, Kawashima T, Stovall M, Leisenring W, Sklar CA, Mertens AC, Donaldson SS, Byrne J, Robison LL. Fertility of male survivors of childhood cancer: a report from the Childhood Cancer Survivor Study. *Journal of Clinical Oncology*. 2010 Jan 10;28(2):332-9.
Green DM, Kawashima T, Stovall M, Leisenring W, Sklar CA, Mertens AC, Donaldson SS, Byrne J, Robison LL. Fertility of female survivors of childhood cancer: a report from the childhood cancer survivor study. *Journal of Clinical Oncology*. 2009 Jun 1;27(16):2677-85.

Fertility Issues After Childhood Cancer Treatment

Adapted from the Children's Oncology Group Health Links

In males, childhood cancer treatment can lead to . . .

Testosterone deficiency. This means that the testicles can't produce enough of the male hormone testosterone. It can be caused by alkylating agent chemotherapy, by radiation therapy to the testicles or the pituitary gland, or by surgical removal of both testicles. If this happens to a young boy, he will need hormones prescribed by a doctor to go into puberty. If it happens after puberty, a man will need testosterone therapy to maintain a healthy body composition of muscle, bone, and fat, as well as a healthy sex drive and the ability to have erections.

Infertility (the inability to father a pregnancy.) Infertility can be caused by reduced testosterone, decreased, damaged, or absent sperm, damage to the duct system that transports the sperm, or to the nerves that control sexual function. There may also be other reasons for infertility that are unrelated to cancer therapy.

For complete information, please see the following Children's Oncology Group Health Link:

<http://www.survivorshipguidelines.org/pdf/MaleHealthIssues.pdf>

In females, childhood cancer treatment can lead to . . .

Estrogen deficiency. Estrogen deficiency is caused when the immature eggs (egg follicles) in the ovaries are depleted or damaged. It can be a result of alkylating agent chemotherapy, radiation therapy to the ovaries or the pituitary gland, or surgical removal of the ovaries. If this happens to a young girl, she will need hormones prescribed by a doctor to go into puberty. Women with depleted egg follicles are at risk of . . .

- Ovarian failure. This means that the ovaries completely stop making estrogen and that menstrual periods stop permanently. Ovarian failure occurs in women at menopause as part of normal aging. The average age of menopause is 51.
- Premature menopause. This means that menstrual periods stop permanently before age 40. If a woman is currently having periods but received chemotherapy or radiation that can affect ovarian function, she may still be at risk of entering menopause at an early age.
- Other health problems. Estrogen is needed to help maintain strong bones, a healthy heart, and overall well-being. Young women who are estrogen deficient should discuss the potential risks and benefits of hormone replacement therapy with their doctor.

Infertility (the inability to get pregnant.) Infertility can be caused by depletion of or damage to egg follicles, and the reduced production of ovarian hormones. Radiation therapy may cause scarring that reduces blood flow to reproductive organs and affects their ability to sustain a pregnancy. There may also be other reasons for infertility that are unrelated to cancer therapy.

Pregnancy risks. Radiation therapy can lead to an increased risk of miscarriage, premature delivery, or problems during labor. Chemotherapy with anthracycline drugs (such as doxorubicin or daunorubicin) and radiation therapy to the upper abdomen or chest may lead to heart problems. If a woman has heart problems, pregnancy and labor can make them worse.

For complete information, please see the following Children's Oncology Group Health Links:

<http://www.survivorshipguidelines.org/pdf/FemaleHealthIssues.pdf>

<http://www.survivorshipguidelines.org/pdf/HeartHealth.pdf>

Is treatment-related infertility permanent?

- Men who had both testicles surgically removed will not be able to make sperm and infertility will be permanent. The same is true for women who had both of their ovaries removed. Infertility following radiation is likely permanent.
- Some men may recover sperm production months or years after the completion of chemotherapy. For others, the damage from chemotherapy may be permanent. **Always assume that you can make someone pregnant unless you are absolutely sure that you cannot!**
- Women who were already menstruating will stop having monthly periods during their cancer therapy. In most cases, menstrual periods will start up again after treatment ends. It can sometimes take up to several years to restart menstruation. **If you don't want to get pregnant, birth control should be used, even if you're not having monthly periods.**
- If a woman is currently having monthly periods and wants to have children but is at risk of premature menopause because of the treatment she received, it is best not to delay getting pregnant beyond the early thirties.

What are the risks to the baby if pregnancy occurs after childhood cancer treatment?

Fortunately, in most cases, there is no increased risk of cancer or birth defects in children born to childhood cancer survivors. In rare cases, if the type of cancer was a genetic (inherited) one, then there may be a chance of passing that type of cancer on to a child. You should check with your oncologist if you are not sure whether the type of cancer you had was genetic.

For more information:

The Society for Reproductive Endocrinology and Infertility - This site provides many fact sheets and booklets that can be downloaded:

<http://www.socrei.org/publications/index.aspx?id=76>