

# Fertility Issues in Childhood Cancer Treatment

Information and Resources for our Families in the  
LPCH Pediatric Oncology Department



# Table of Contents

- I. Introduction**
- II. What are possible effects of cancer therapies on my child's reproductive system?**
- III. Questions to ask your doctor before therapy**
- IV. Factors that affect the risk of infertility**
  - a. Common cancers in childhood and adolescence**
  - b. Chemotherapy**
  - c. Radiotherapy**
  - d. Information for hematology patients receiving bone marrow transplants**
- V. Before therapy: Options for protecting fertility**
- VI. After therapy: Important health and social issues**
- VII. Additional resources**
- VIII. Important contact information**



**Introduction** After your child has been diagnosed with cancer, survival is your first concern. While medical advances have helped most children survive cancer, treatments for cancer may cause side effects. Infertility, or the inability to have children, is a side effect of some cancer therapies. Even though your child's future fertility may not be a main concern at the time of diagnosis, there are ways to help protect their chances to have children in the future. It is important to check into these options before starting treatment. It is also important to be aware of the effects of cancer treatment on future child-bearing to know what to expect after completion of therapy.

The goal of this booklet is to offer the most up-to-date information on both the infertility risk (based on your child's disease and treatment) as well as options to save fertility that are available at Lucile Salter Packard Children's Hospital and in the nearby area. We hope that the information in this booklet will help you to understand your child's risks and options, so that you can make a decision that is best for your family. **Please be sure to talk with your child's health care provider about any questions or concerns.**

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*Dr. Stewart McCallum, Stanford Urologist, Male Infertility Specialist*

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## **What are possible effects of cancer treatment on the reproductive system?**

Cancer therapies can affect hormone production and the ability to have children in different ways. The following is a list of possible effects on fertility caused by cancer treatment:

***Delayed or Early Puberty:*** During puberty a girl or boy starts to develop adult physical changes. For a girl this usually happens between the ages of 8 and 13 years and for a boy this usually happens between the ages of 10 to 15 years. The first signs of puberty are usually the growth of breast buds in females and testicular enlargement in males. However, hair under the arms and in the pubic areas may be the first thing that you will notice because it is usually a more noticeable change. Children who have been treated for cancer can have a delayed or an early (precocious) start to puberty. Children who have to take hormone therapy to go through puberty are at risk for infertility. An endocrinologist, a specialist who treats problems with glands that make hormones, can do tests to find out if hormone therapy is needed to help puberty go on at a normal rate and time.

***Infertility (females):*** For females, infertility occurs when there is damage to the eggs, uterus, fallopian tubes, or ovaries. Women are born with all of the eggs that they will have for their lifetime. Cancer treatment can damage some or all of these eggs. Because women are born with all of their eggs, they cannot be replaced. This is the main cause of infertility in young women who have been treated for cancer.

***Infertility (males):*** For males, infertility usually occurs because the sperm are low in number or are no longer being made due to effects of the cancer treatment on the testicles. Infertility in males can also be caused by damage to the cells in the testes that make the male hormone, testosterone (see below for more details about Leydig cell dysfunction). Men who have already gone through puberty can check their fertility after cancer treatment by giving a semen sample at the California Cryobank (see the contacts section).

***Leydig Cell Dysfunction (males):*** Chemotherapy and radiation that injure the Leydig cells can result in low levels of testosterone. Low testosterone levels may reduce sex drive and result in problems with sexual functioning. Testosterone is also an important hormone for bone health. Men with low testosterone levels may have thinner, weaker bones (osteoporosis). Hormone therapy may be needed in men who have low testosterone levels. If blood tests show a low testosterone level after cancer treatment, your doctor may also order a bone density test to check bone strength. If bone strength is lower than normal, getting enough calcium and vitamin D (in the diet or by taking a supplement), exercising regularly, and not smoking can help keep bones strong and healthy in men with low levels of testosterone. The treatments that are more likely to cause Leydig cell dysfunction are shown in the table on page 8.

***Premature ovarian failure:*** Normally women go through menopause (natural ovarian failure that occurs with aging) after 40 years of age. The average age is 51 years old. However, some female patients go through *premature ovarian failure*, or early menopause, during or after cancer treatment. In one large study at 5 pediatric cancer centers, the average age for menopause was 31 years old for young women treated for cancer with certain chemotherapies and radiation to the abdomen. In women who have had cancer treatment, early menopause is a sign of infertility. It is important for a young woman who wants to have children in the

future to plan child-bearing based on her risk of early menopause. This could include storing eggs to use later. Some signs of early menopause include hot flashes, mood swings, night sweats, and irregular periods with little or no bleeding. In early menopause, the levels of hormones made by the ovaries are low. Women who go through early menopause should discuss the risks and benefits of taking hormone therapy with their doctor. Low levels of ovarian hormones also increase the risk of bone thinning (osteoporosis). Getting enough calcium and vitamin D (in the diet or by taking a supplement), exercising regularly, and not smoking can help keep bones strong and healthy in women who go through early menopause.

## **Questions to ask your doctor before therapy**

Even though your child may be many years away from having children of his or her own, thinking about his or her fertility before starting cancer treatment can help increase the chances of being able to have children in the future. Talk to your medical team about how your child's therapy will affect fertility. Below are some possible questions to ask your doctor:

- Will treatment have any short or long term side effects on my child's reproductive system?
  - Will the treatments affect hormone levels that control puberty and the ability to have children?
  - Is there any chance of having puberty start earlier or later than kids who do not have cancer treatment?
  - Is infertility a possible side effect of treatment?
- Are there other ways to treat the cancer that will cause less damage to the reproductive system?
- Are there ways to save (preserve) fertility before, during and after cancer treatment?
- Do treatments that preserve fertility work as well against the cancer as those that cause infertility?
- After treatment, how will I know if I will be able to have children?
- How can a girl find out if she is at risk to enter menopause early?

## Factors that affect the risk of infertility

The risk of infertility varies for different types of cancers and cancer treatments. The tables below give an estimate of the possible risk of infertility based on studies of childhood cancer survivors who are now adults. The risk of infertility after specific childhood cancers and cancer treatments may be high, medium, or low to none. Based on the risk, you can decide whether or not you would like to look into ways to preserve your child's fertility before starting cancer treatment.

<b>Infertility risk based on common cancers of childhood and adolescence</b>
<b>High risk:</b> Any cancer or hematologic illness treated with bone marrow transplantation Hodgkin's disease treated with 6 or more months of alkylating drugs Soft-tissue and Ewing's sarcoma that has spread to distant organs (metastatic)
<b>Medium risk:</b> Acute myeloid leukemia Hepatoblastoma Osteosarcoma Ewing's sarcoma that has not spread to distant organs or tissues Soft-tissue sarcoma that has not spread to distant organs or tissues Neuroblastoma Non-Hodgkin lymphoma Hodgkin's disease treated with 3 or less months of alkylating drugs Brain tumor treated with radiation to brain and/or spine
<b>Low to no risk:</b> Acute lymphoblastic leukemia Wilms' tumor Germ-cell tumors that are not treated with radiation Retinoblastoma Brain tumor treated with surgery only or low dose radiation to brain

**Infertility risk based on chemotherapy treatment**

**High Risk:**

Chemotherapy conditioning for bone-marrow transplantation

Cyclophosphamide above 4,000 mg/m<sup>2</sup> for males

Cyclophosphamide above 15,000 mg/m<sup>2</sup> for females

Ifosfamide

Mechlorethamine

Busulfan

Melphalan

Procarbazine

Chlorambucil

*Specific Regimens:* MOPP, COPP/ABV

**Medium Risk:**

Cyclophosphamide below 4,000 mg/m<sup>2</sup> for males

Cyclophosphamide below 15,000 mg/m<sup>2</sup> for females

Cisplatin

Carboplatin

Doxorubicin

*Specific Regimens:* VAMP w/COP

**Low Risk/No Risk:**

Cytarabine

Vincristine

Methotrexate

Dactinomycin

Bleomycin

Mercaptopurine

Vinblastine

<b>Risk of infertility based on radiation treatment</b>
<p><b>High Risk Males:</b></p> <p>Pelvic radiation</p> <p>Testicular radiation</p> <p>Cranial radiation with high or medium risk chemotherapy</p>
<p><b>High Risk Females:</b></p> <p>Ovarian or pelvic radiation</p> <p>Cranial radiation with high or medium risk chemotherapy</p>
<b>Risk of Leydig cell dysfunction (low testosterone) based on radiation</b>
<p>Pelvic or testicular radiation</p> <p>Medium or high risk chemotherapy in boys who have gone through puberty (<i>see page 3 for more information on Leydig cell dysfunction</i>)</p>

*All risk table information has been estimated based on discussions with practicing physicians and the following article: Wallace WH, Anderson RA, Irvine DS. Fertility preservation for young patients with cancer: who is at risk and what can be offered? Lancet Oncol 2005;6(4):209-18. **Please discuss the risk levels with your doctor.***

## Before therapy: Options for protecting fertility

Families and patients often ask what can be done before treatment begins to protect future fertility. Your doctor can tell you if the risk of infertility is low based on the cancer treatments planned. In these cases, special procedures to protect fertility are not needed. If the risk of infertility is medium or high, you may want to check into options that will help preserve fertility. The different options will depend on whether the patient has or has not gone through puberty. The chart below describes potential options for each age group and sex, followed by definitions and explanations of these terms.



	Girls	Boys
Before puberty	Ovarian shielding Ovarian transposition	Testicular shielding
	<i>Experimental options:</i> Hormone therapy Ovarian tissue cryopreservation	<i>Experimental option:</i> Testicular Tissue Freezing (TTF)
After puberty	Ovarian shielding Ovarian transposition Embryo Cryopreservation	Sperm banking Testicular shielding Embryo cryopreservation
	<i>Experimental options:</i> Hormone therapy Oocyte cryopreservation Ovarian tissue cryopreservation	

### Definitions from table:

*Oocyte Cryopreservation:* For girls who have already gone through puberty, oocyte cryopreservation (egg freezing) is a good option. While this is still a new, experimental procedure, it has resulted in successful pregnancies. The procedure involves stimulating the ovaries with fertility medications that are given by injection into a muscle for two weeks. During this time, the patient's ovaries are monitored by ultrasound every 1 to 3 days. When the eggs have developed to the right stage, they are removed during a short outpatient procedure by inserting a needle into the ovaries. The eggs can be stored until the woman is ready to become pregnant. At this time, the eggs are fertilized with sperm from a partner or donor and the embryo that develops is then inserted into the uterus. To date, about 200

pregnancies have been achieved with this technique. If your family is interested in this option, please make an appointment with Dr. Lynn Westphal (see contacts section).

*Embryo Cryopreservation:* Embryo cryopreservation (embryo freezing) is a proven, safe option for preserving fertility. Eggs are harvested from the ovaries in a process similar to that described above in the egg freezing procedure. Like the egg freezing procedure, this procedure often involves stimulating the ovaries with fertility medications that are given by injection into a muscle for two weeks. During this time, the patient's ovaries are monitored by ultrasound every 1 to 3 days. The eggs are then fertilized with sperm from a partner or donor and the embryo that develops is frozen. The embryo is frozen until the woman is ready to start a family. The fertilized egg is placed into the uterus through an IVF (in-vitro fertilization) procedure. This procedure is a very safe, ultrasound guided procedure that helps infertile couples to conceive every day. It is important to keep the timing in mind when deciding on this treatment option. The first pregnancy from a frozen embryo was in 1983, and since then thousands of children have been born following embryo freezing. Today, most centers show about a 20-30% success rate of term pregnancy per embryo stored. Often times many embryos are stored to increase the chance of pregnancy. If you are interested in this option your family should contact Dr. Lynn Westphal (see contacts section).

*Hormone therapy:* Some studies have shown that giving a hormone called GnRH to girls, or the hormones in birth control pills to women, may reduce the risk of damage to the ovaries caused by cancer treatments. Other studies have not shown a benefit in preserving ovarian function in women who received these treatments. Because not all patients have been helped by these treatments, using medicines like GnRH and birth control pills to save fertility is controversial. You should discuss the risks and benefits of these treatments with your oncologist, gynecologist, or endocrinologist.

*Ovarian Tissue Cryopreservation:* This is an experimental procedure that involves the surgical removal of a piece of ovarian tissue. To date, only 1 to 2 pregnancies have been reported after using this technique. This procedure is an option for girls who have not gone through puberty or for girls who can not wait the 2 weeks to start treatment that is required for egg or embryo freezing. The piece of ovarian tissue is frozen until after treatment when the patient is ready to have children. In successful trials, the ovarian tissue has been put back into the pelvis by a brief, simple outpatient surgery. When the ovarian tissue is put back into the body, the hope is that it will begin to function like normal ovarian tissue. If the transplanted ovarian tissue produces hormones normally, this procedure can reduce the risk of early menopause and infertility.

*Ovarian Transposition:* This is a method used to reduce damage to the ovaries during pelvic radiation for Hodgkin's disease and other cancers that require radiation in the pelvis. Surgery is done to move the ovaries to another area of the body to help protect them from the radiation treatment. After therapy is complete, the ovaries can be moved back to their original location. After treatment for some cancers, the ovaries remain in the new location and can still function normally. If pelvic radiation is part of your child's treatment, please talk to your oncologist about this option. It is also possible to perform ovarian tissue harvesting at the same time as this procedure. Please contact Dr. Lynn Westphal (see contacts section) if you are interested in learning more about this procedure.

*Ovarian/Testicular Shielding:* Radiation shielding is routinely done in children treated with abdominal or pelvic radiation, unless the shielding will increase the chances of cancer relapse. For boys, the doctor will place lead-lined shields over one or both testicles. For girls, shields are placed over one or both ovaries. This may help reduce the risk of damage to the testicles or ovaries during treatment. These methods are only used for radiation and not for chemotherapy. This is something that your radiation oncologist will be able to talk to you more about.

*Sperm Banking:* This is a simple way for boys who have gone through puberty to preserve fertility before treatment. This is recommended for all male patients who are at high or medium risk for infertility. Semen samples can be collected as frequently as every day before starting cancer treatment and stored for future use. This is a worthwhile option even if only one deposit can be given, or even if the sperm count is low. The sample can remain frozen indefinitely. There is a sperm bank located across the street from LPCH called California Cryobank (see contacts section).

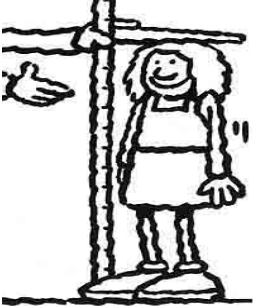
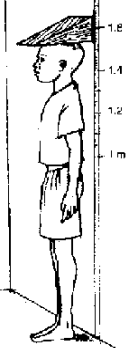


*Testicular Tissue Freezing (TTF):* This is an option for boys who have not gone through puberty and cannot provide a sperm sample. The procedure involves an outpatient surgery to remove a small amount of tissue from the testicles and freeze it for future use. There have been no live births reported in boys who have undergone testicular tissue freezing, so the procedure is still considered experimental. Dr. Stewart McCallum (see contacts section) can perform this surgery at Stanford Hospital. For more information about this procedure please ask your oncologist and/or set up an appointment directly with Dr. McCallum

## After therapy: Important health and social issues

Once cancer therapy is completed and remission is achieved, staying healthy is important to assure that survivors live a long time and with a good quality of life. Regular check-ups by your oncology team and a primary care physician are important to check for late effects of cancer treatment. All of your health care providers should know about your child's past cancer treatment so they can monitor for treatment side effects.

The list below shows topics to review with your doctor after therapy:

	Girls	Boys
Before puberty	<ul style="list-style-type: none"> <li>• Check growth and puberty</li> </ul> 	<ul style="list-style-type: none"> <li>• Check growth and puberty</li> </ul> 
After puberty	<ul style="list-style-type: none"> <li>• Check growth and puberty</li> <li>• Menstrual history</li> <li>• Measure hormone levels (FSH, LH, estrogen)</li> </ul>	<ul style="list-style-type: none"> <li>• Check growth and puberty</li> <li>• Semen analysis (sperm count and motility)</li> <li>• Measure hormone levels (testosterone, DHT)</li> </ul>

### Other important considerations after treatment:

*Sexually-transmitted diseases and unplanned pregnancies:* Whether or not cancer treatment is given that may affect fertility, it is important to advise childhood cancer survivors about the risk of sexually-transmitted diseases and unplanned pregnancies. Practicing safe sex is important for everyone to reduce the risk of sexually-transmitted diseases. Some studies have shown that cancer survivors may think they are not able to have children and then have an unplanned pregnancy. Childhood cancer survivors should be counseled about measures to take to avoid sexually-transmitted diseases and unplanned pregnancies.

*Pregnancy and parenthood after cancer:* Studies so far have shown that most children born to cancer survivors have no greater risk for birth and genetic defects than children born to individuals who have not had cancer. Most children of cancer survivors also do not have higher rates of getting cancer themselves. However, some rare forms of cancer are hereditary or can "run in families". These may occur in individuals who have cancer in both sides of paired organs (for example eyes, ears, breasts, kidneys, etc.) or who have many family members with cancer (the same or different types). If you are not sure whether or not your child's cancer type is a hereditary type, ask your oncologist. Female cancer survivors who

have had cancer treatments that can affect heart function, or radiation to the abdomen and pelvis should be aware that they may have a higher risk of complications during pregnancy, labor or delivery. Women who have had these cancer treatments should consult with their doctor before becoming pregnant. Please keep in mind that there are many ways to become a parent, including adoption, surrogacy, and donor eggs and sperm.

*Sperm Extraction:* Some men who find out after treatment that they do not have sperm in the ejaculate, will still have sperm available in the testes or stored in a nearby collecting structure called the epididymis. These men can have the sperm aspirated or extracted in a minor out-patient procedure. The extracted sperm can then be frozen for later use.

## **Additional resources**

If you would like to learn more information about fertility issues and cancer, the following websites offer extensive information:

### **Fertility Issues:**

1. *FertileHope*: Through programs of awareness, education, financial assistance, research and support, Fertile Hope is providing cancer survivors with the tools they need to fulfill their parenthood dreams. Online resources include message boards, informational packets, and news updates on research advances and advocacy efforts. For more information, please call (888) 994-HOPE or visit [www.fertilehope.org](http://www.fertilehope.org).



2. *Lance Armstrong Foundation*: [www.livestrong.org](http://www.livestrong.org)

### **Late Effects of Cancer Treatment Health Information:**

1. *Children's Oncology Group (COG) Survivorship Guidelines*  
Male: [www.survivorshipguidelines.org/pdf/MaleHealthIssues.pdf](http://www.survivorshipguidelines.org/pdf/MaleHealthIssues.pdf)  
Female: [www.survivorshipguidelines.org/pdf/FemaleHealthIssues.pdf](http://www.survivorshipguidelines.org/pdf/FemaleHealthIssues.pdf)  
Other late effects topics: [www.survivorshipguidelines.org](http://www.survivorshipguidelines.org)

2. *Premature Ovarian Failure Support Group*: [www.pofsupport.org/](http://www.pofsupport.org/)

## Important contact information

**Female infertility specialist** (ovarian tissue and egg freezing), Stanford Hospital:  
Lynn Westphal, M.D., Lisa Murray, R.N. (650) 498-7272

**Male infertility specialist** (testicular tissue freezing), Stanford Hospital:  
Stewart McCallum, M.D. (650) 723-5546

**Pediatric Endocrinology, LPCH** (hormone issues, early/delayed puberty):  
Laura Bachrach, M.D., Patricia Fechner, M.D., and Kirk Neely, M.D.

**Please fax referral form to: 650-725-8379**

### California Cryobank

Location: Stanford Barn 700 Welch Road, Suite 107  
(650)-324-1900

For almost 30 years California Cryobank has been the leader in reproductive tissue services. California Cryobank has a dedicated staff to help patients with their storage needs and we strongly believe in helping every patient preserve their fertility. **No patient will be turned away.** California Cryobank has a tradition of assisting patients financially and helps each patient on a case by case basis. For that same reason, patients from Packard Hospital receive an immediate 15% discount off our storage services. In addition, California Cryobank participates in the Care Credit program ([www.carecredit.com](http://www.carecredit.com)). For more information, patients may call our Palo Alto office at 650-324-1900. Patients may also visit our website at [www.cryobank.com](http://www.cryobank.com) for further information.



Citations:

Fertile Hope: Childhood Cancer and Fertility: A Guide for Parents. [www.fertilehope.org](http://www.fertilehope.org)

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Nicholson HS, Byrne J. Fertility and pregnancy after treatment for cancer during childhood or adolescence. *Cancer* 1993;71(10 Suppl):3392-9.

The Infertility Center of St. Louis (St. Luke’s Hospital) website: [www.infertile.com](http://www.infertile.com)

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