Liddy Shriver Sarcoma Initiative

Cancer and Fertility

An ESUN Article

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Introduction

There have been great improvements in the survival of cancer patients, including those with sarcoma, over the past few decades. However, along with improved survival, permanent side effects like infertility are often a result. The good news is that more fertility preservation and parenthood after cancer options exist now than ever before. For men and women, there are several options before and after cancer treatments.

Approximately 130,000 cancer patients are diagnosed each year during their reproductive years. Up to 90% of these men and women may be at risk of permanent infertility due to treatments like chemotherapy, radiation and surgery, yet less than 10% of oncologists inform all eligible patients about their fertility risks and fertility preservation options.

What is unique about the needs associated with cancer and fertility is that they are solvable. Compared to all of the big issues in cancer, fertility is easy – there are risks and there are solutions. The goal of this article is to better educate you on cancer-related infertility so that you can help solve this problem. The impact of your efforts will be profound. At a high level, we will have forever changed the practices of the cancer and reproductive communities. At an individual level, cancer survivorship will transcend generations.

Cancer Survivor’s Perspective

Being diagnosed for the second time with tongue cancer at the age of 24 was daunting. For me, Lindsay Nohr Beck, however, cancer was the easy part. I beat it before and was confident that I would beat it again. The discussions of permanent side effects like infertility were more overwhelming.

Similar to the majority of oncologists, my doctor did not inform me of my risks. Later I asked and was shocked to learn that my treatment regime did have a high probability of rendering me infertile and that it would definitely cause me to enter menopause early. I went on a quest to find a way to preserve what was sacred to me—my fertility.

As a single young woman, embryo freezing was not an option—I did not have a partner and did not want to use donor sperm. When I questioned my vast team of physicians, called fertility clinics, scoured the Internet and reached out to cancer and fertility organizations about the
possibility of freezing unfertilized eggs (oocyte cryopreservation), I came up empty handed.

Refusing to give up, I reached the point of repeatedly calling the same places. On my third attempt to Stanford Medical Center, I was finally told that an egg-freezing program was available, but only for young cancer patients. For the first time in my life, I was happy to be the "young cancer patient"! There was finally hope.

Time was of the essence. I had to start chemotherapy in two weeks and egg freezing takes approximately 12-14 days. I was immediately examined, advised of the costs, risks and procedural details and sent home with a bag of medicine. After two weeks of self-administered shots, intense side effects and an outpatient surgical procedure, my eggs were safely stored.

I now had a tangible piece of hope—something to live for, to fight for. I started chemotherapy and radiation on time and finished treatments with a secret excitement for what the future would bring.

I got lucky. I stumbled across the right person with the right information at the right time. While these treatments came with their own risks, they promised something chemotherapy couldn’t—a chance at reproduction. Every young cancer patient should have that chance, and it shouldn’t require luck.

Four years later, I am a newlywed excited to start a family with my husband—and we are both grateful to have so many parenthood options.

Definitions

Infertility: Infertility is considered to be present for a couple when no pregnancy has occurred after one year of attempted intercourse. In many couples where an infertility problem is suspected, evaluation and/or treatment should be considered before the year of attempted conception. For men, infertility is the inability to father a child. In general, this is when you no longer make sperm or the sperm are very few in number or are damaged by prior cancer treatment. Infertility is not the same as impotence, which involves sexual functioning. For women, infertility occurs when you no longer produce mature eggs for ovulation or have some other condition that prevents you from getting pregnant or maintaining a pregnancy. You are born with a certain amount of eggs in your ovaries. Some of the eggs will be damaged and destroyed from cancer treatments. Because eggs do not regenerate, this loss can cause infertility and premature ovarian failure.

Premature Ovarian Failure: Premature ovarian failure (or early menopause) is the loss of fertility before age 40. Some women go into menopause immediately after treatment, which also means that they are infertile. Other women get their periods again and are fertile. Even if a woman’s period returns, her egg supply may have been damaged so she may experience infertility or enter menopause early. If a woman goes into menopause early, she may need to take calcium supplements and hormone replacements, like the birth control pill. Some cancers, especially breast and uterine tumors, are hormone sensitive, so it is important to consult with an oncologist to determine how best to treat premature ovarian failure in their young patients.

Fertility Risks

Cancer treatments affect the body in different ways. Chemotherapy, radiation and surgery can all affect your reproductive system (Ref. 1). The following are factors to consider:

- Patient age
- Type of drug(s)
- Dose of drug(s)
- Location and amount of radiation
- Location and scope of surgery

Cancer

Cancer itself can cause infertility. For example, some men with testicular cancer and Hodgkin's disease have low sperm counts before treatment even starts (Ref. 2). There is no evidence that men diagnosed with sarcomas have infertility before treatment, unless the sarcoma affects the testes directly or causes a blockage of sperm flow (e.g., prostate, retroperitoneal or bladder sarcomas).

Chemotherapy

Chemotherapy can damage developing cells like sperm and eggs. Chemotherapy drugs in the alkylating class are the most destructive. Individual treatment factors like patient age, drug type, drug combinations and total drug dose affect the chance of becoming permanently infertile and/or experiencing premature ovarian failure.

Radiation

Radiation can also damage the reproductive system (Ref. 3). If the radiation field includes the brain, it may affect fertility by damaging areas that control hormone production. Radiation therapy aimed close to, or at the pelvic areas of the body, can also cause infertility by directly damaging the testes or ovaries. Individual treatment factors of location and dose affect the chance of becoming infertile.

Surgery

Surgery that removes part or all of your reproductive system can cause infertility (Ref. 4). If your cancer involves your testicles, ovaries, uterus, cervix or the nerves and lymph nodes in the abdomen and pelvis, talk to your doctor about the effects of the surgery on your fertility and/or your ability to carry a baby. Treatments like bone marrow and stem cell transplants that involve high doses of radiation and chemotherapy present a high risk of infertility. Other medical treatments may also damage fertility. Accordingly, it is important for the patient and medical team to work together to understand the importance of fertility to the patient and the potential risks of their cancer treatments.

Men

An overview of available options for men is summarized in the following table.

<table>
<thead>
<tr>
<th>Fertility Options for Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
</tr>
</tbody>
</table>

"Cancer and Fertility" in the Sarcoma Learning Center http://sarcomahelp.info/learning_center/articles/fertility.html
Fertility Preservation Options Before Treatment

Sperm Banking

Sperm banking is a simple, proven way to try to preserve your fertility. Sperm may be frozen and "banked" for future use (Ref. 5). Sperm samples can be collected as frequently as daily or every other day to be cryopreserved (frozen). Even if your sperm count is low or you only have time to make one deposit, sperm banking may still be worthwhile. There are new technologies that require fewer sperm to achieve pregnancy. Once the sperm is frozen, there is no limit as to how long it can remain frozen until it is used.

Testicular Tissue Freezing

Testicular tissue freezing is an option for some men who cannot bank sperm because of the inability to ejaculate, or for boys who are prepubescent. When sperm are present in the testicle but not in the semen, sperm-bearing tissue can be removed surgically from the testicles and freeze it for future use (Ref. 6). This procedure is often offered to men who have no sperm in the ejaculate at the time of diagnosis, although it is typically performed at centers with both reproductive and oncology activities. Testicular tissue freezing is still considered experimental for prepubescent boys, since the frozen tissue does not contain fully developed sperm.

Radiation Shielding

Radiation shielding is when special shields are placed over one or both of the testicles to help
reduce the risk of damage to fertility. It does not protect against chemotherapy (Ref. 7).

**After Treatment Diagnosing Infertility**

A semen analysis is a simple test that can be performed by a doctor after treatment to see if a man is producing sperm (Ref. 8). The results of the test will help determine the best options for becoming a father. Sometimes sperm production will start again after treatment. This usually happens within two years after treatment, but some patients become fertile again years later. Birth control is advised for those who are not ready to have children.

**Parenthood Options After Cancer**

**Natural conception** is an option if the sperm analysis is in the normal range. Many cancer survivors have children naturally after treatment. Many oncologists suggest that a patient wait a year before trying to conceive because sperm may be damaged by the treatment and an increased risk of birth defects in children may occur early after chemotherapy or radiation. In addition to the damage to sperm genetic material, cancer treatment may cause a decrease in sperm production. The decrease in sperm production from cancer treatments may take one to six years to wear off. Following semen analyses during this period may be considered to monitor the process of recovery of sperm production.

**Assisted reproduction** may be an option for men whose sperm analysis is low or shows no sperm after treatment. If the patient banked sperm, it can be used with intrauterine insemination (IUI), in vitro fertilization (IVF) or IVF-ICSI to try to achieve pregnancy. If sperm wasn’t banked, a procedure called testicular sperm extraction (TESE) may be performed to try to find residual sperm in the testicular tissue (Refs. 9, 10, and 11). The chances of success with TESE run approximately 40%, but varies considerably based on the chemotherapy used and/or the specific type of tumor treated.

**Donor sperm** from another man can be used if no sperm is found in either the semen or testicular tissue. Sperm donation programs allow men to select an anonymous donor whose traits and characteristics closely match their own (Ref. 12).

**Adoption** is an excellent choice for anyone wanting to become a parent. Adoption agencies may look at your medical history or require a letter from the oncologist about the patient’s health and/or require a certain amount of time to pass since your diagnosis before allowing a cancer survivor to adopt. Accordingly, it is a good idea to select an agency that is open to working with cancer survivors (Ref. 13).

**WOMEN**

An overview of available options for women is summarized in the following table.
<table>
<thead>
<tr>
<th>Fertility Options for Women</th>
<th>Age</th>
<th>Average Cost</th>
<th>Time Requirement</th>
<th>Success Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Embryo Freezing</strong></td>
<td>After puberty</td>
<td>$7,800; $350/year storage fees</td>
<td>2 - 4 weeks</td>
<td>Approximately 40% per 3 embryos transferred under 35; lower in older women</td>
</tr>
<tr>
<td><strong>Egg (Oocyte) Freezing</strong></td>
<td>After puberty</td>
<td>$8,000; $350/year storage fees</td>
<td>2 - 4 weeks</td>
<td>Experimental; approximately 3% per egg frozen</td>
</tr>
<tr>
<td><strong>Ovarian Tissue Freezing</strong></td>
<td>Before and After Puberty</td>
<td>$12,000; $350/year storage fees</td>
<td>Outpatient Surgical Procedure</td>
<td>Experimental; one live birth to date</td>
</tr>
<tr>
<td><strong>Ovarian Transposition</strong></td>
<td>Before or After Puberty</td>
<td>Unknown</td>
<td>Outpatient Surgical Procedure</td>
<td>Approximately 50% for ovarian function, pregnancy rates unknown</td>
</tr>
<tr>
<td><strong>Radical Trachelectomy</strong></td>
<td>Before or After Puberty</td>
<td>Unknown</td>
<td>Inpatient Surgical Procedure</td>
<td>Experimental</td>
</tr>
<tr>
<td><strong>GnRH Analog Treatment</strong></td>
<td>After puberty</td>
<td>$500 per dose</td>
<td>1 dose per month in conjunction with chemotherapy</td>
<td>Experimental; study results vary: some show no benefit, others show success</td>
</tr>
<tr>
<td><strong>Donor Embryos</strong></td>
<td>Varies, usually 18-25+</td>
<td>$5,000-$7,000 in addition to IVF costs</td>
<td>2 - 6 weeks per cycle</td>
<td>Unknown, similar to that of frozen embryo IVF transfers</td>
</tr>
<tr>
<td><strong>Donor Eggs</strong></td>
<td>Varies, usually 18-25+</td>
<td>$14,000 - $20,000</td>
<td>2 - 4 weeks per cycle</td>
<td>ART with Egg Donation, 40-50%</td>
</tr>
<tr>
<td><strong>Surrogacy</strong></td>
<td>Varies, usually 18-25+</td>
<td>$10,000 - $100,000</td>
<td>Varies</td>
<td>Similar to IVF, 20-30%</td>
</tr>
</tbody>
</table>
Fertility Preservation Options Before Treatment

Embryo Freezing *

Embryo freezing is a proven, successful way to preserve a woman’s fertility. It requires sperm, so it is a good option to consider for women who are married, have a partner or are willing to use donor sperm. The process requires hormonal stimulation for approximately two weeks as well as a minor procedure under general anesthesia to retrieve the eggs. The eggs are then fertilized in the lab and frozen for future use. The process takes two to six weeks, and is dependent on the patient’s menstrual cycle. Pregnancy rates per transfer (generally 2-4 embryos are transferred at once) range from 20-40% depending on the center and patient’s age—millions of babies have been born worldwide from embryo freezing.

Egg Freezing *

Egg freezing is still experimental, but may be a good option to consider for single women who do not want to use donor sperm. Pregnancy rates are lower than embryo freezing (unfertilized eggs are more delicate and can easily be damaged during cryopreservation), but the techniques are improving. The process is the same as embryo freezing except that once the eggs are removed they are frozen unfertilized. The pregnancy rates per egg from egg freezing range 1-3%—less than 150 pregnancies have been reported worldwide from this technique.

*For egg and embryo freezing, alternative stimulation protocols are available if the cancer is hormone sensitive (e.g. in association with endometrial adeno cancers). For example, instead of being stimulated with standard fertility medications, Letrozole can be used to stimulate the ovary to mature multiple eggs for retrieval. These protocols are still experimental and should be discussed with both an oncologist and reproductive endocrinologist to determine if they are safe for the patient.

Ovarian Tissue Freezing

Ovarian tissue freezing is the most experimental option of the three. It may be a good option to consider if the patient does not have a lot of time before treatment, if hormone stimulation is unsafe or if the patient is pre-pubertal. Ovarian tissue is removed laproscopically, sliced into small strips and frozen for future use. Later, the tissue can be re-implanted into the body (usually the arm or the pelvis) where hormone function can be restored and eggs can develop. The eggs can then be removed, fertilized with sperm and implanted into the patient’s uterus (or the uterus of a gestational surrogate) to try to achieve pregnancy. Ovarian tissue freezing is a one-day outpatient procedure and, to date, there has been one baby born worldwide.
Ovarian Shielding & Ovarian Transposition

These are methods of minimizing radiation to the ovaries and, accordingly, can decrease the amount of damage to the ovaries and the eggs. These options do not protect against chemotherapy and often come with their own risks. For example, ovarian transposition can inadvertently cut off the blood supply to the ovaries resulting in loss of function.

Fertility Sparing Surgery

For cancers present in the reproductive area, there are now several fertility sparing surgeries. In
the recent past, sarcomas and other cancers in the uterus were treated with a full hysterectomy; however, today there are now many surgical options for gynecologic cancers that may help preserve your fertility. Women with sarcoma in the reproductive region who are concerned with fertility may be able to consider fertility-sparing surgical options.

**After Treatment Diagnosing Infertility**

Women who are having periods without the aid of hormonal supplements like birth control pills, may be fertile after treatment. Again, however, menstruation is not equivalent to fertile, so it is important to see a reproductive endocrinologist to perform hormone tests and pelvic ultrasounds to measure the approximate number of egg reserve in the ovaries (Ref. 14). The results of these tests will help determine which parenthood options are most appropriate. Moreover, most women don’t realize that even if they are in menopause, they can carry a pregnancy.

**Parenthood Options After Cancer**

**Natural Conception**

Natural conception may be possible after treatment. Many women are able to get pregnant naturally after cancer treatments (see "An Update on Planet Cancer," by Heidi Adams, in the April 2005 issue of ESUN).

**Assisted Reproduction**

Assisted reproduction methods like embryo freezing, egg freezing and ovarian tissue freezing, are usually thought of as pre-treatment options; however, they can also be done after cancer treatment. If a woman resumes menstruation, but is afraid that she will go into menopause before she is ready to start a family, these techniques can be used to preserve fertility after treatment.

These treatments can also be used for women who resume menstruation and/or have signs of fertility after cancer treatments, but are having difficulty getting pregnant naturally. Generally, the definition of infertility is to try to conceive unsuccessfully for one year. After six months to a year of trying, cancer survivors might want to work with a reproductive endocrinologist to better understand the cause of trouble and determine best practices for moving forward.

**Donor Eggs & Embryos**

Donor eggs and embryos can be used if a woman does not have any more healthy eggs after treatment. Egg donation allows her to select an anonymous donor whose traits and characteristics closely match her own. The donor eggs can be fertilized with her partner’s sperm to create embryos and implanted into her uterus (or the uterus of a gestational surrogate) to try to achieve pregnancy. Embryo donation is when couples that created embryos but have completed their own families donate them to other couples for use (Ref. 15). Embryo donation is less common that egg donation, but both are somewhat less regulated than adoption and can be easier for a cancer survivor to pursue.
Gestational Surrogacy

Gestational surrogacy is when another woman carries a baby for you. This may be an option if the oncologist feels that pregnancy is unsafe or if the woman is unable to carry a child. If the patient is not in early menopause, her eggs can be fertilized with sperm and implanted into a surrogate. The surrogate would then carry her biological child. If she cannot use your own eggs, donor eggs or embryos can be used. Surrogacy laws vary from state to state (e.g. in some states it is illegal), so it is important to understand the surrogacy laws where you live.

Adoption

Similar to the above section for men, adoption is an excellent choice for anyone wanting to become a parent. Adoption agencies may look at your medical history or require a letter from the oncologist about the patient’s health and/or require a certain amount of time to pass since your diagnosis before allowing a cancer survivor to adopt. Accordingly, it is a good idea to select an agency that is open to working with cancer survivors (Ref. 16).

Safety of Pregnancy & Children After Cancer

Current available studies suggest the following:

- Pregnancy after cancer does not reduce chances of the patient’s survival (i.e. trigger cancer recurrence), even after breast cancer.
- Radiation to the uterus can increase the risk of miscarriage or premature births.
- The stress of pregnancy can sometimes worsen undetected damage from cancer treatment to a woman’s heart or lungs.
- Sperm cells exposed to chemotherapy or radiation may suffer genetic damage. This damage appears to be repaired within one year after treatment.
- Growing eggs exposed to chemotherapy or radiation may suffer genetic damage. This damage appears to be repaired within six months.
- Rates of birth defects in the general population are 2% to 3%. Rates of birth defects in children born after one parent’s cancer treatment appear similar; no higher than 6% and probably less.
- No unusual cancer risk has been identified in the offspring of cancer survivors (except in families identified with true genetic cancer syndromes, for example, inherited retinoblastoma).

Research thus far is reassuring, but the number of pregnancies and births studied after cancer treatment is still small; larger studies could reveal additional health risks. Please consult your medical team when considering conception and pregnancy after cancer.

Sample Questions for Patients to Ask Physicians

1. Will my treatment have any short or long term side effects on my reproductive system?
2. Is infertility a possible side effect of my treatment?
3. Are there alternative ways to treat my cancer that will result in less damage to my reproductive system?
4. What are my fertility preservation options before, during and after treatment?
5. Would using any of these options possibly make my cancer treatment less effective?
6. After treatment, how will I know if I am infertile?
7. After treatment, will I enter into menopause prematurely?
   (women only)
8. If I become menopausal after this treatment, is the change more likely to be temporary or permanent?
   (women only)
9. If I become infertile after treatment, what are my options for becoming a parent?
10. How long after treatment should I wait before trying to conceive?

About Fertile Hope

Founded in 2001, Fertile Hope is a national nonprofit organization dedicated to providing reproductive information, support and hope to cancer patients whose medical treatments present the risk of infertility. Through programs of awareness, education, financial assistance, research and support, Fertile Hope is empowering cancer patients and survivors with the tools they need to fulfill their parenthood dreams. Whether you are a physician, nurse, social worker, mental health professional, patient or survivor, Fertile Hope has resources for you to make navigating the reproductive world easier. Fertile Hope's resources include:

Cancer & Fertility Brochures

- Cancer & Fertility
- Breast Cancer & Fertility
- Young Adults Guide to Cancer & Fertility

Cancer & Fertility Resource Guide

Fertile Hope recently launched the second edition of its Cancer & Fertility Resource Guide as a tool to help healthcare professionals, patients and survivors locate fertility services that can help cancer survivors become parents. The guide is free and includes:

- Educational information written by world renowned experts
- Comprehensive physician and service listings by state
- Twenty unique categories of services ranging from in vitro fertilization and sperm banking to surrogacy and adoption

Fertile Hope’s Website
Fertile Hope’s website offers a unique tool that outlines the risks that treatments like chemotherapy, radiation and surgery present to the reproductive system. It also provides an overview of fertility preservation and parenthood options before, during and after cancer treatments, allowing you to compare options by age, time required, average success rates and cost. All of Fertile Hope’s resources are also available to download or order for free on their website.

**Sharing Hope – Fertility Preservation Financial Assistance Program**

Cancer patients have little opportunity to save and budget for the immediate high costs of cancer, let alone any procedures or treatments intended to help preserve their fertility. Cancer patients often have a small window of opportunity between diagnosis and treatment in which they may pursue these options, and the upfront costs are often prohibitive. The goal of Fertile Hope’s Sharing Hope program is to increase access to such procedures and treatments for qualified men and women diagnosed with cancer in their reproductive years. Through the program, Fertile Hope offer assistances for qualified male and female applicants by providing the following:

- Discounted sperm banking services from GIVF Cryobanks
- Access to fertility medications donated by Serono, Inc.
- Discounted egg and embryo freezing services from reproductive endocrinologists from across the country

The Sharing Hope program does not itself grant financial contributions, but instead has aligned with key organizations to make egg, embryo and sperm freezing more accessible.

**Speakers Bureau**

Fertile Hope recently launched a Cancer & Fertility Speakers’ Bureau with the goal of coordinating presentations at cancer centers around the country. Contact us if you would like more information about having Fertile Hope present at your center.

**References**


3. Ibid.


7. "Recommendation for the use of specific area gonad shielding on the patient," FDA Center for Devices and Radiological Health, Sec.

"Cancer and Fertility" in the Sarcoma Learning Center http://sarcomahelp.info/learning_center/articles/fertility.html
8. "What tests are used to diagnose male infertility?" University of California Davis Health System


12. "Fertility After Cancer…Options for Starting a Family," Virtual Hospital, The University of Iowa Hospitals and Clinics

13. Ibid.


15. "Fertility After Cancer…Options for Starting a Family," Virtual Hospital, The University of Iowa Hospitals and Clinics.

16. Ibid.

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