

## **Fertility Concerns for Cancer Survivors**

Survival remains the primary focus of cancer treatment; however, technological advances have improved survival rates for many cancers resulting in a large population of long-term survivors and more emphasis on quality of life concerns. Fertility following cancer treatment is one focus of recent widespread attention. Each year, thousands of individuals in the United States will be diagnosed with cancer before or during their reproductive years. In addition, more individuals are delaying having children for personal and/or professional reasons. Therefore, these numbers are likely to continue increasing.

Several recent surveys indicate that the majority of cancer survivors with no children would like to have children in the future and many who already had children would like to have more. Many survivors felt that their experience with cancer made family relationships and parenthood more valuable to them. Most would like to have biological children and were worried about their fertility. However, many patients felt that they did not receive adequate information about future fertility and felt that this information would be important at the time of diagnosis and treatment decision-making.

This very broad, complicated topic encompasses a variety of concerns including the effects of cancer treatments on fertility, available fertility preservation options, cancer risks associated with fertility treatments and pregnancy, and risks of birth defects and cancer among children of cancer survivors. Therefore, we will divide this topic into sections.

### **Effects of Cancer Treatment on Fertility**

A brief outline of the fertility risks associated with different cancer treatments follows. These risks vary based on individual factors (i.e. age, sexual maturity) and factors related to the type of cancer and treatment (i.e. cancer site and stage, types of treatment, dose, etc.). Therefore, individuals should discuss the risks and benefits of their personal cancer treatment options with their healthcare providers in order to make informed decisions.

#### **Fertility Risks**

##### **Chemotherapy**

Chemotherapy drugs often work by targeting rapidly dividing cells; however, these cells include both cancer cells and some normal healthy cells. Chemotherapy can cause immediate infertility or reduced fertility by damaging sperm, egg, and/or hormone-producing cells. In addition, even those women who do not experience immediate infertility after chemotherapy are at risk for menopause at an earlier than expected age and a shorter than normal period of fertility due to reduction in the overall ovarian reserve (number of egg-containing follicles). Higher risks of infertility are associated with older age at treatment, higher total dose, and treatment with certain classes of drugs (particularly alkylating agents).

##### **Radiation**

Radiation also works by targeting rapidly dividing cells; however, its effects are limited to tissues in or around a targeted area. Radiation to the abdominal or pelvic region or total body irradiation (TBI) may damage the uterus, ovaries, or testicles resulting in infertility and/or pregnancy complications (miscarriage, premature delivery, low birth weight). Radiation to certain areas of the brain may also result in infertility by affecting hormone production. Location, dose, fractionation schedule, and age at treatment affect the risk of infertility.

### Surgery

Surgery to remove part or all of the reproductive organs may cause infertility and/or pregnancy complications. Risk depends on the organs affected and the extent of surgery.

## **Fertility Preservation Options**

The following is an outline of the existing methods for fertility preservation. The feasibility, safety, and suitability of fertility preservation options differ for each individual depending on a number of variables including their gender, age, type of cancer and treatment, and whether or not they have a partner. The cost, availability, risks, and success rates of fertility preservation techniques also vary. Therefore, individuals should discuss the risks, benefits, and limitations of the available fertility preservation options with their healthcare providers in order to make informed decisions.

### For Women:

#### Embryo Freezing

- Collection of mature eggs, fertilization in vitro (combining egg and sperm in a laboratory dish to allow fertilization to occur), and freezing of fertilized embryos for future use
- Traditionally involves hormone stimulation for egg retrieval (Women are given certain hormones to stimulate their ovaries to produce several eggs. Egg development is monitored by ultrasound and when mature, eggs are collected using a needle guided by ultrasound or laparoscopic surgery.)
- Recent success with alternative stimulation drugs including tamoxifen and aromatase inhibitors may make this procedure safer for patients with hormone sensitive tumors (i.e. endometrial and breast cancer)
- Requires partner or donor sperm and a minimum of ~12-14 days for egg collection
- One of the most successful techniques available

#### Egg (Oocyte) Freezing

- Collection of mature eggs and freezing of unfertilized eggs for future use
- For women who do not have a partner and do not wish to use donor sperm
- Requires a minimum of ~12-14 days for egg collection and stimulation as above
- Experimental, limited success but techniques improving

#### Ovarian Tissue Freezing

- Surgical removal, division into small pieces, and freezing of ovarian tissue for later transplantation back into the woman's body
- Experimental, but recent progress including restoration of ovarian hormonal function (at least for a short time) and reports of a couple of successful pregnancies in women who had transplantation of previously thawed ovarian tissue
- *However, much more data demonstrating the success and safety of these procedures will be necessary before they are routinely available clinically.*

#### Gonadotropin Releasing Hormone (GnRH) Analog Treatment

- Treatment with GnRH analogs during chemotherapy theoretically creates a temporarily pre-pubertal state which may reduce damage to reproductive tissues and therefore reduce the risk of infertility
- Experimental, variable data on success
- *Most studies show no effect and therefore suggest that this should not be relied on as the only means of fertility preservation*

#### For Men:

##### Sperm Banking

- Donation and freezing of sperm cells prior to the start of treatment
- Usually involves the collection of several sperm samples over a ~5-8 day period
- Generally a relatively simple, inexpensive, and effective technique; however, success rates vary depending on sperm quality and quantity
- Certain types of cancer, particularly testicular cancer, impair sperm quality such that it may be suboptimal even prior to treatment
- Advances in reproductive technology have improved success even with low sperm quality and/or quantity

##### Testicular Sperm Extraction

- For pre-pubertal men who do not have adequate mature sperm present in their semen
- Testicular tissue is surgically removed and sperm are retrieved and used immediately or frozen for future use
- Requires use of expensive, specialized assisted reproduction techniques due to limited number of sperm
- Success rates are variable but encouraging
- Considered experimental for use in prepubertal boys with premature sperm cells

##### Testicular Tissue Freezing

- Experimental procedure involving surgical removal, freezing, and storage of testicular tissue including sperm-producing cells
- No reported successful births resulting from sperm cells retrieved in this manner to date

Other options for fertility preservation or parenthood include less extensive surgery for early-stage gynecologic cancers, movement of the ovaries out of the field of radiation to minimize damage if pelvic radiation is necessary for treatment, use of donor sperm, eggs, or embryos, surrogacy, or adoption.

### **Concerns about risks of fertility treatments to cancer survivors and their children**

This section will address some common concerns including the potential risks to children born following cancer treatment and risks for the cancer survivor associated with fertility preservation techniques and pregnancy. We will review available information regarding the risks for cancer and birth defects in children of cancer survivors and children conceived using assisted reproductive technologies (ART) (fertility preservation/infertility treatment techniques).

#### **Risk of Birth Defects and Cancer Among Children of Cancer Survivors**

Surveys indicate that many cancer survivors are interested in having children after treatment for cancer. However, they often fear that their past cancer treatment will increase their risk of having a child with a birth defect and/or that their children will be at high risk for cancer. Fortunately, although the data are somewhat limited, current research suggests that children of cancer survivors are not more likely to have birth defects or chromosome abnormalities. In addition, multiple studies have shown that *in the absence of a hereditary cancer syndrome* children of cancer survivors do not appear to have a higher overall rate of cancer development.

#### **Health Risks Among Children Conceived Using Assisted Reproductive Technologies**

As the use of assisted reproductive technologies increases, questions have also been raised about the long-term safety (in terms of health and development) for children conceived using these techniques. Many of these techniques are still very new; therefore, long-term data is limited. However, the available data shows little evidence of an overall increased risk of birth defects or developmental problems; if there is any increased risk for specific health or developmental problems, it is likely small. One important exception is the high rate of multiple births (e.g. twins, triples, etc.) resulting from use of ART and their association with a higher rate of complications for the mother and infants including low birth weight, prematurity, infant death, cerebral palsy, and developmental delay. There also appears to be a higher rate of prematurity, low birth weight, and infant death even among single children conceived using these techniques. There does not appear to be a higher rate of childhood cancer among children conceived using these techniques.

#### **Risk Associated with Fertility Treatments and Pregnancy for Cancer Survivors**

Cancer survivors often express fear that fertility preservation treatments or subsequent pregnancies will increase their risk of cancer recurrence and/or decrease their survival. Again, data are still somewhat limited and some controversy still exists, particularly with respect to hormone sensitive tumors (e.g. breast cancer). However, current studies have not shown an increased risk of recurrence or a decrease in survival with pregnancy following adequate treatment for cancer (including breast cancer). In addition, the available data suggests that existing fertility preservation techniques do not decrease the

success of cancer treatment. However, individual circumstances must be considered when choosing appropriate fertility preservation techniques including the potential for a delay of treatment and the hormone sensitivity of the tumor. The optimal timing of pregnancy following a cancer diagnosis and treatment is not clear but many suggest a waiting period of ~2-5 years to ensure that treatment has been successful, thus decreasing the likelihood of a recurrence during pregnancy.

One potential risk for female cancer survivors is an increase in pregnancy complications. Current data show a lower rate of live births and a higher rate of low birth weight babies, prematurity, and miscarriage among female cancer survivors. This is especially true for women treated with radiation to the pelvis, head, spine, or total body. This is thought to result from harmful effects on the structure and/or function of the uterus and/or the function of the hormonal systems which are necessary to maintain pregnancy. There is also a higher rate of miscarriage, prematurity, and low birth weight babies among women who receive conservative surgery (e.g. removal of part or all of the cervix but not the uterus) for low gynecologic cancers (e.g. cervical cancer). An additional concern for female cancer survivors is that pregnancy may aggravate organ damage caused by cancer treatment. Of particular concern is the potential risk for cardiovascular problems for women treated with chest radiation and/or certain types of chemotherapy. For these reasons, all female cancer survivors who become pregnant should be considered at increased risk for pregnancy complications and be followed by specialized perinatal care.

**Additional sources of information about fertility concerns for cancer survivors:**

[www.fertilehope.org](http://www.fertilehope.org)

Fertile Hope is a national nonprofit organization that provides information and support to cancer survivors concerned about infertility. The website provides clear, simple answers to frequently asked questions and includes a list of questions for patients to ask their doctors about cancer treatment and fertility. It also provides a support network and information about financial support for fertility preservation/infertility treatment.

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

People Living With Cancer ([www.plwc.org/patientguides](http://www.plwc.org/patientguides))

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