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# Female Fertility and Cancer

Cancer and its treatment can sometimes affect a woman's ability to have children. Learn how cancer surgery and treatment can affect fertility, ways to help preserve fertility, and possible fertility options available after treatment.

- How Cancer and Cancer Treatment Can Affect Fertility in Females
- Preserving Fertility in Females with Cancer

# How Cancer and Cancer Treatment Can Affect Fertility in Females

What can cause fertility problems

It's very important to talk to your cancer care team to know how a cancer surgery or treatment that's being recommended for you may affect your fertility **before** having the surgery or starting treatment. If these problems aren't talked about before surgery or treatment, it's important that they are brought up as soon as possible after surgery or when treatment starts. **Don't assume your doctor or nurse will ask you about fertility concerns.** Read more about talking with your health care team in <a href="How Cancer and Cancer Treatment Can Affect Fertility">How Cancer and Cancer Treatment Can Affect Fertility</a>. You need to be sure to get enough information, support, or resources to help you deal with any doubts, feelings, and expected fertility problems.

Fertility refers to having the ability to conceive, or being able to have a child. For

females, fertility means they are able to become pregnant through normal sexual activity, and they are able to carry the baby through pregnancy. A person's fertility depends on their reproductive organs working properly and other factors, such as when and how often they are having sex, certain hormones, and if their partner has any problems with fertility.

When a person cannot have a child, this is called **infertility**, or being infertile. For females, infertility can mean they are not able to get pregnant through normal sexual activity or they have problems carrying a baby through pregnancy. Doctors usually consider someone to be infertile if they haven't been able to conceive a child after 12 or more months of regular sexual activity, or after 6 months if the female is more than 35 years old.

Problems with fertility can also be called **reproductive problems**or**alterations**. They happen when certain hormone levels are abnormally low or high or if sex organs are removed or aren't working properly. Some people never find out why they are having fertility problems. Many experts believe stress and anxiety can cause changes that play a part in infertility.

This information is for females with cancer. **If you are a lesbian or a transgender person**, please talk to your cancer care team about any needs that are not addressed here.

### What can cause fertility problems

When a couple makes (conceives) a baby, this is called **conception**or **reproduction**. When a baby is conceived naturally, a lot of things must take place for it to happen. For example, we know a female is born with all the eggs she will ever have and they're stored in her ovaries. Any change in how the ovaries work, or a change in a hormone that's needed to release an egg from the ovary during monthly cycles (called **ovulation**), can cause conception not to happen. In other words, there can be a "body system malfunction" that can change a woman's fertility and affect her ability to get pregnant and carry a child through a pregnancy. Certain health problems, including cancer, can affect these things.

Females can be diagnosed as infertile if:

- The ovaries don't contain healthy eggs
- Hormones that are needed to help with egg release are disrupted
- A tumor or other problem might press on the ovaries or uterus (womb) and cause them not to work properly

- Damage to other parts of the reproductive system prevents eggs from being released, fertilized, or implanted
- A fertilized egg cannot grow inside the uterus
- Something happens that won't allow a fetus (unborn child) to be carried through the full pregnancy, causing a miscarriage

In many cases, cancer surgery or treatments can be more likely than cancer itself to interfere with some parts of the reproductive process and affect your ability to have children. Different types of surgeries and treatments can have different effects. The risk of infertility varies depending on:

- The patient's age and stage of development; for example, before or after puberty, before or after menopause, etc.
- The type and extent of surgery
- The type of treatment given (radiation therapy, chemotherapy, hormone therapy, targeted therapy, immunotherapy, stem cell transplant)
- The dose of treatment

#### Surgery

Surgery might be needed for a tumor that's in or near another reproductive organ, such as an ovary or fallopian tube, or the uterus or cervix. It might also be needed for a tumor that's in nearby abdominal (belly) or pelvic organs, such as the colon, rectum, or anus. There are some tumors that happen near the nervous system, such as the brain or spinal cord. These surgeries may affect a woman's fertility.

#### Surgery to remove reproductive organs

A **hysterectomy** is surgery to remove the uterus. Since an unborn child is carried in the uterus, once the uterus is removed, a woman cannot get pregnant. In females with cancer, removal of the uterus is done for <u>uterine (endometrial) cancer</u><sup>2</sup>, <u>cervical cancer</u><sup>3</sup>, and often for other cancers that affect the reproductive system.

An **oophorectomy**is surgery to remove the ovaries. It might be done at the same time as a hysterectomy. Since ovaries hold a woman's eggs, a woman can't get pregnant without them. For females with cancer, an oophorectomy is done for <u>ovarian cancer</u><sup>4</sup>, and often for other cancers that affect the reproductive system. If possible, and if there is a low risk that the cancer will come back, the surgeon might try to save one ovary to preserve eggs, which might still allow a woman to become pregnant. Keeping at least

one ovary also preserves the hormones that help prevent menopause symptoms like hot flashes and vaginal dryness. Some women at high risk for breast, uterine, and ovarian cancers choose to have an oophorectomy as a means to help prevent the cancers from starting.

A **trachelectomy**is surgery to remove the cervix (lower part of the uterus). It leaves the uterus behind so a woman has the chance to carry a pregnancy.

These surgeries can be done either through the vagina (laparoscopy) or through a cut (incision) made in the abdomen. You might hear people refer to a "partial" or "tota" hysterectomy. This usually means the procedure only removes the uterus (partial) or it removes all reproductive organs (total).

Some women at high risk for breast, uterine, and ovarian cancers, or who have a hereditary cancer syndrome might choose to have a partial or total hysterectomy as a means to help prevent the cancers from starting.

might survive if the ovaries are moved further from the target area in a minor surgery to preserve them that might be able to be done before radiation begins.

Fertility depends on the female's stage in life (before or after puberty, before or after menopause), menstrual history, hormone levels, the type of cancer and treatment, and the treatment doses. Because all these factors need to be considered, it can be hard to predict if a woman is likely to be fertile after chemo.

Chemo drugs that are linked to the **risk of infertility** in females are:

- Busulfan
- Carboplatin
- Carmustine
- Chlorambucil
- Cisplatin
- Cyclophosphamide
- Cytosine arabinoside
- Doxorubicin
- Ifosfamide
- Lomustine
- Melphalan
- Mitomycin-C
- Nitrogen mustard (mechlorethamine)
- Procarbazine
- Temozolomide
- Thiotepa
- Vinblastine
- Vincristine

Higher doses of these drugs are more likely to cause permanent fertility changes, and combinations of drugs can have greater effects. The risks of permanent infertility are even higher when females are treated with both chemo and radiation therapy to the belly (abdomen) or pelvis.

Some other chemo drugs that have a **lower risk** of causing infertility in females include:

- 5-fluorouracil (5-FU)
- 6-mercaptopurine (6-MP)
- Bleomycin
- Cytarabine
- Dactinomycin
- Daunorubicin

other harm. Some can contribute to having a miscarriage. Some women remain fertile during chemo, so it's best to use very effective birth control. Remember, too, that some women can get pregnant even when their periods have stopped. For this reason, it's important to use birth control whether or not you have periods, but talk to your cancer care team about what's best for your situation.

If you remain fertile through treatment and want to get pregnant after it ends, be sure you know how long you should wait before trying. Studies about this are hard to find, but some suggest getting pregnant too soon after chemo can harm the fetus, cause birth defects, or cause a woman to miscarry

See Chemotherapy<sup>8</sup> for more information.

#### Hormone therapy

Hormone therapies<sup>9</sup> are often used to treat breast cancer or other cancers. These can affect your ability to have a child. Some of these drugs, such as tamoxifen, might not cause problems getting pregnant, but can cause birth defects. Other hormone therapies may block or suppress hormones, causing infertility by putting a woman into early menopause. This may be temporary or permanent, depending on the type and length of treatment.

It's always best to talk to your cancer care team about your treatment and any possible effects on your sexual function and fertility. It's also very important to talk about whether you need to use birth control during and after treatment.

#### Targeted therapy and immunotherapy

Targeted therapy and immunotherapy drugs attack cancer cells differently from standard chemo drugs. Little is known about their effects on fertility or problems during pregnancy. It's very important to talk to your doctor about any targeted or immunotherapy drugs you will get, and the fertility risks that might come with them, and any precautions that might be needed. Some information is known, such as:

- Bevacizumab (Avastin<sup>®</sup>) can cause ovarian failure, and some women's ovaries never recover.
  - Some targeted drugs (thalidomide and lenalidomide) have such a high danger of causing

See <u>Targeted Therapy</u><sup>10</sup> and <u>Immunotherapy</u><sup>11</sup> to learn more about these cancer treatments.

#### Bone marrow or stem cell transplant

Having a bone marrow or stem cell transplant usually involves receiving high doses of chemo and sometimes radiation to the whole body before the procedure. In most cases, this permanently stops ovaries from releasing eggs, resulting in lifelong infertility. Talk with your doctor or nurse about th0 1gmost

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# Preserving Fertility in Females with Cancer

- Fertility preservation for females with cancer
- Possible natural pregnancy
- Cryopreservation (freezing embryos or eggs)
- Ovarian transposition
- Fertility-sparing surgery
- Options for women who are not fertile after cancer treatment

Certain cancers and their treatment can affect fertility in males and females. Read more about this in <u>How Cancer and Cancer Treatment Can Affect Fertility</u><sup>1</sup>. When a person with cancer wants to have children after treatment ends, some planning is needed. Sometime this involves **fertility preservation**. Fertility preservation is when eggs, sperm, or reproductive tissue are saved or protected so that a person can use them to have children in the future.

This information is for females with cancer. **If you are a lesbian or transgender person**, please talk to your cancer care team about any needs that are not addressed

here.

#### Fertility preservation for females with cancer

Certain types of cancer surgery can result in removal of organs needed for a pregnancy, and certain treatments might change hormone levels or cause damage to a female's eggs. These effects result in some females losing their fertility during treatment that can be either temporary or permanent. Read more in How Cancer and Cancer Treatment Affect Can Fertility in Females. Some women may choose to take steps that might help preserve their fertility so they can try to have children after treatment.

It's best that discussions about preserving fertility take place before cancer surgery happens or before treatments begin. **Don't assume your doctor or nurse will ask you if fertility is important to you.** They don't always remember to bring this up, so you might have to bring it up yourself.

If you are considering taking steps to preserve your fertility, and it's possible to do so, be sure that you understand the risks and chances of success of any fertility option you are interested in, and keep in mind that no method works 100% of the time.

It's also very important to talk to your cancer care team about if you can have unprotected sex both during and after cancer treatment. They may recommend waiting a number of months or longer before trying to have a child by natural means or until resuming unprotected sexual intercourse.

Experts recommend doctors who are part of the cancer care team be involved in talking about fertility with patients, including medical oncologists, radiation oncologists, gynecologic oncologists, urologists, hematologists, pediatric oncologists, surgeons, nurses, and others. The experts have the following recommendations:

- The cancer care team should talk about any possible fertility problems that might happen due to treatment as early as possible, either before surgery or before treatment starts.
- Patients who are interested in fertility preservation, might be thinking about it, or want to learn more, should be referred to a reproductive specialist.
- The cancer care team should start talking about preserving fertility as early as possible, too, meaning before treatment starts.
- Referrals to counseling should be made for people who may be anxious or distressed about fertility-related effects.

Learn more about how you can start talking about fertility with your cancer care team in How Cancer and Cancer Treatment Can Affect Fertility<sup>2</sup>.

## Possible natural pregnancy

In females who were fertile before treatment, the body may recover naturally after treatment. It may be able to keep or restore normal hormonal cycles. and produce

If you have frozen eggs, embryos, or ovarian tissue, it's important to stay in contact with the cryopreservation facility to be sure that any yearly storage fees are paid and your address is updated.

#### **Embryo freezing**

Embryo freezing, or embryo cryopreservation, is an effective way to help preserve fertility for females. Mature eggs are removed from the female and put in a sterile lab dish with several thousand sperm. The goal is for one of the sperm to then fertilize the egg. This is called **in vitro** fertilization (IVF). **In vitro intracytoplasmic sperm injection** (IVF-ICSI) involves taking a single sperm and injecting it directly into an egg to fertilize it. In both IVF and IVF-ICSI, the lab dish is observed and if the egg is fertilized, the embryo can be frozen. Later, after treatment ends and the woman is ready to try to get pregnant, the embryo is thawed and put back into the female's uterus to try to achieve a pregnancy.

A woman's age and menopause status plays a large role in the chances of pregnancy, with a younger age at the time of egg retrieval resulting in higher potential for pregnancy. The quality of the embryos also makes a difference. Some may not survive the thawing process. Some may not implant into the uterus correctly.

#### Egg (oocyte) freezing

Egg freezing (or oocyte cryopreservation) is also an effective way to help preserve fertility for women, although it has not been used as long as embryo freezing (described above). This may be a good choice for women who do not have a partner, do not want to use donor sperm to make a fertilized embryo, or if they have a religious conflict with freezing a fertilized embryo.

For egg freezing, mature eggs are removed from the female and frozen before being fertilized with sperm. This process might also be called **egg banking**. When the woman is ready to try to become pregnant, the eggs can then be thawed, fertilized by a partner's or donor's sperm, and implanted in her uterus to try to achieve pregnancy.

#### **Ovarian tissue freezing**

This procedure is still experimental. It involves all or part of one ovary being removed by laparoscopy (a minor surgery where a thin, flexible tube is passed through a small cut near the navel to reach and look into the pelvis). The ovarian tissue is usually cut into small strips, frozen, and stored. After cancer treatment, the ovarian tissue can be thawed and placed in the pelvis (transplanted). Once the transplanted tissue starts to

function again, the eggs can be collected and attempts to fertilize them can be done in the lab.

Ovarian tissue removal does not usually require a hospital stay. It can be done either before or after puberty.

#### **Ovarian transposition**

Ovarian transposition means moving the ovaries away from the target zone of radiation treatment. It's a standard option for girls or young females who are going to get pelvic radiation. It can be used either before or after puberty.

This procedure can often be done as outpatient surgery and does not require staying in the hospital (unless it is being done as part of a larger operation). Surgeons will usually move the ovaries above and to the side of the central pelvic area. It's usually best to do the procedure just before starting radiation therapy, since they tend to fall back into their normal position over time.

The success rates for this procedure vary. Because of radiation scatter, ovaries are not always protected, and patients should be aware that this technique is not always successful.

It's hard to estimate the costs of ovarian transposition, since this procedure may sometimes be done during another surgery that is covered by insurance.

# **Fertility-sparing surgery**

For early-stage cervical cancer, the surgeon can sometimes <u>remove the cervix</u><sup>3</sup> (trachelectomy) without removing the entire uterus or ovaries. For early-stage <u>ovarian</u> <u>cancer</u><sup>4</sup> that only affects one ovary, the surgeon might be able to remove the one ovary that's affected and not the other. Both of these procedures can help preserve fertility. See the images below for more information.

#### Ovarian suppression

Gonadotropin-releasing hormone (GnRH) agonists are long-acting hormone drugs that can be used to make a woman go into menopause for a short time. This is called ovarian suppression. The goal of this treatment is to shut down the ovaries during cancer treatment to help protect them from damaging effects. The hope is that reducing activity in the ovaries during treatment will reduce the number of eggs that are damaged, so women might be able to resume normal menstrual cycles after treatment.

their doctors to carry a pregnancy but cannot conceive with their own eggs. The process involves *in vitro* fertilization (IVF) (see above).

Donated eggs come from women who have volunteered to go through a cycle of hormone stimulation and have their eggs collected. In the United States, donors can be known or anonymous. They can be paid or unpaid. Some women have a sister, cousin, or close friend who is willing to donate her eggs without payment. There are also frozen egg banks available from which women can purchase frozen eggs that are then sent to a fertility center for IVF.

Per regulations, egg donors are carefully screened for sexually transmitted infections and genetic diseases. Every egg donor should also be screened by a mental health professional familiar with the egg donation process. These screenings are just as important for donors who are friends or family members. For known donors, everyone also needs to agree on what the donor's relationship with the child will be, and be certain that the donor was not pressured emotionally or financially to donate her eggs.

The success of the egg donation depends on carefully timing hormone treatment (to prepare the lining of the uterus, if it's safe to give) to be ready for an embryo to be placed inside. The eggs are taken from the donor and fertilized with the sperm. Embryos are then transferred to the recipient to produce pregnancy. Continued hormone support might be needed until the placenta develops and can produce its own hormones.

It's important that you research the experience and success rates of the IVF or fertility center you may use.

#### **Donor embryos**

A woman who has a healthy uterus and can maintain a pregnancy may be given the option to have in vitro fertilization (IVF) (see above) with donor embryos. These donated fertilized eggs do not have sperm or the egg of the couple trying to get pregnant. This approach lets a couple experience pregnancy and birth together, but neither parent will have a genetic relationship to the child. Embryo donations usually come from a couple who has had IVF and has extra frozen embryos.

One problem with this option is that the couple donating the embryo may not agree to have the same types of genetic testing as is usually done for egg or sperm donors, and they may not want to supply a detailed health history. On the other hand, the embryos are usually free, so the cost to the cancer survivor involves the process to make the uterus ready to accept the embryo and having the embryo placed. But, there can be legal and medical fees that mount up.

Most women who use the donor embryo procedure must get hormone treatments to prepare the lining of the uterus and ensure the best timing of the embryo transfer. So, they must be able to safely take hormones.

It's important that you research the experience and success rates of any IVF or fertility center you may use.

#### Surrogacy

Surrogacy is an option for women who cannot carry a pregnancy, either because they no longer have a working uterus, or would be at high risk for a health problem if they got pregnant. There are 2 types of surrogate mothers:

- A gestational carrier is a healthy female who receives the embryos created from the egg and sperm of the intended parents or from egg or sperm donors. The gestational carrier does not contribute her own egg to the embryo and has no genetic relationship to the baby.
- A **traditional surrogate** is usually a woman who becomes pregnant through artificial insemination with the sperm of the male in the couple (or a sperm donor) who will raise the child. She gives her egg (which is fertilized with his sperm in the lab), and carries the pregnancy. She is the genetic mother of the baby.

Surrogacy can be a legally complicated and expensive process. Surrogacy laws vary, so it's important to have an attorney help you make the legal arrangements with your surrogate. You should consider the laws of the state where the surrogate lives, the state where the child will be born, and the state where you live. It's also very important that the surrogate mother be evaluated and supported by an expert mental health professional as part of the process. Very few surrogacy agreements go sour, but when they do, typically this step was left out.

#### Adoption

Adoption is usually an option for many people who want to become a parent. Adoption can take place within your own country through a public agency or by a private arrangement, or internationally through private agencies. Foster care systems and other agencies specialize in placing children with special needs, older children, or siblings.

Many adoption agencies or foster care systems state that they do not rule out cancer survivors as potential parents. But they may require you to be done with treatment, and likely will need some information about your type of cancer and quality of life. You may

be able to find an agency that has experience working with cancer survivors. Cancer survivors have some legal protections (including against discrimination during adoption proceedings) under the Americans with Disabilities Act (ADA).

There's a lot of paperwork to complete during the adoption process, and at times it can seem overwhelming. Many couples find it helpful to attend adoption or parenting classes before adopting. These classes can help you understand the adoption process and give you a chance to meet other couples in similar situations. The process takes different lengths of time depending on the type of adoption you choose.

Costs of adopting vary greatly, from around \$6,000 (for a public agency, foster care, or special needs adoption) up to \$35,000 to \$50,000 (for private U.S. and some international adoptions, including travel costs).

You might be able to find an agency that has experience working with cancer survivors. Some discrimination clearly does occur both in domestic and international adoption. Yet, most cancer survivors who want to adopt can do so.

#### **Child-free living**

Many couples, with or without cancer, decide they prefer not to have children. Child-free

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