Male Fertility and Cancer Treatment

Cancer and its treatment can affect a man’s chance of fathering a child. Being able to father a child is known as fertility. It is vital to speak openly with your care team about how your cancer and treatment plan could change your fertility.

What is male fertility and how can cancer treatment affect it?

A man needs to be able to make healthy sperm to be able to father a child. Sperm grow and mature in the seminiferous tubules, which are in the testicles. A man has two testicles, located in the scrotum. Semen is the fluid that sperm live in. Sperm is always being made, making them a target for chemotherapy damage. Before puberty there is no sperm being made. Germ cells (precursors to sperm) are still there and reproducing, making them a target of chemotherapy as well. Germ cells and sperm can also be harmed by radiation, even in low doses.

Another group of cells in the testes are the Leydig cells. The job of these cells is to make the male sex hormone, testosterone. Without testosterone, a boy may not achieve puberty. An adult male with low testosterone may have loss of secondary sex traits (facial hair, mature genitals and deep voice) or abnormal sexual functioning. Leydig cells can be harmed by radiation, but are not as sensitive to it as sperm and germ cells. Leydig cells are not often harmed by chemotherapy. Having azoospermia (absence of sperm in the semen) due to damage to the germ cells, does not affect sexual function.

The pituitary gland, found in the brain, makes hormones (LH and FSH). These stimulate the testes to make sperm and testosterone. Radiation therapy to the brain can damage the pituitary gland, affecting sperm and testosterone production.

Cancer itself can cause men to have poor sperm quality, even before treatment. About 40% of men with Hodgkin’s disease and 50% with testicular cancer will have low sperm counts at the time of diagnosis. Fortunately, advances in fertility preservation (discussed later in this article) have allowed men with poor sperm to father children after treatment.

Chemotherapy and Fertility

Chemotherapy works by killing quickly dividing cells. These can be cancer cells or normal cells. Many cells in our bodies are quickly dividing, like those lining the gut, hair follicles, and germ cells (including sperm and oocytes or eggs). When these cells are damaged by chemotherapy, it causes side effects. These include diarrhea, mouth sores, hair loss, and the ability to have children.

It is very hard to figure out which men will become infertile as a result of chemotherapy treatments. The effects depend on the type and number of chemotherapy drugs received, as well as the total dose. The group of chemotherapies called alkylating agents are known to really effect sperm being made, but this depends on the dose. Other chemotherapies that greatly affect sperm being made are chlorambucil and cyclophosphamide when given alone and procarbazine and cisplatin in high doses, among others. In some cases, an often used regimen may be changed to protect a man’s fertility.

Azoospermia (no sperm) or oligospermia (low sperm count) may not be permanent. It can take from months to years for sperm production to recover. Sperm counts are typically lower after chemotherapy. There can also be damage to the genetic makeup (DNA) of sperm after chemotherapy. Research has found that this damage is repaired after therapy is done, though it isn’t clear how long this takes.

Each situation is unique. You should speak openly with your care team about the chemotherapy you are getting and how it could change your fertility. Ask your care team how long you should wait after your chemotherapy is done before fathering a child. The effect on fertility is not yet known for many newer types of chemotherapy and other cancer therapies, such as targeted and immune therapies.
Radiation and Fertility

Radiation is the use of high energy x-rays to kill cancer cells and can affect your fertility. Radiation to the testicles, or body parts near the testicles, can damage the cells that make sperm. The chance of infertility after radiation depends on the dose to the testes, shielding, and fractionation (single dose vs. multiple doses). Smaller doses can lead to a temporary inability to make sperm. Higher doses can lead to permanent infertility (inability to make sperm). Leydig cells are less sensitive to the effects of radiation, but damage can still happen.

There are two ways to try to prevent fertility issues from radiation treatment. If the testicles are not the target, shielding can be used. This protects the testicle(s) from being exposed to radiation. Fractionation divides the total dose of radiation into many smaller doses. Fractionation is used to lessen most side effects. In the case of fertility, fractionation (many smaller doses) causes more damage to sperm than a larger, single radiation dose.

Total body irradiation (TBI) is used before stem cell and bone marrow transplants. As the name suggests, it is radiation of the whole body. About 80% of men who have TBI will have permanent azoospermia. Shielding is not a choice in this type of radiation.

For those with temporary azoospermia after radiation, sperm counts are at their lowest 4-6 months after treatment. Counts often return to their pretreatment levels 10-24 months after treatment. This can take longer in those who got higher doses of radiation.

Surgery and Fertility

If a cancer surgery requires the removal of both testes, fertility is affected because of the inability to make sperm. Surgery on the prostate, bladder, urethra, or colon can result in a condition called retrograde ejaculation. In normal ejaculation, the semen is sent through the urethra (the same tube that carries urine from the bladder), and the opening to the bladder closes off, letting the semen leave the penis. In retrograde ejaculation, the opening to the bladder does not close, allowing the semen to enter the bladder instead of exiting the penis. While this is not harmful, it does impair fertility.

If a man still makes sperm, is there any danger or risk to fathering a child after therapy?

A common concern is if a child will have birth defects caused by exposure of sperm to cancer therapies. Studies have found no increase in birth defects in the children of cancer survivors. Nor do these children have higher rates of cancer (this does not include families with genetic cancer syndromes).

The DNA of sperm can be damaged by cancer therapies, but this damage repairs itself. You should speak with your care team before fathering a child after treatment for cancer.

Options for Fertility Preservation

Sperm banking

Cryopreservation (freezing & storage) of sperm is the only proven method of fertility preservation in men. This frozen sperm is later used to fertilize a woman’s egg using in-vitro fertilization (IVF) or, in some cases, injected directly into the woman’s uterus. For many men with cancer, sperm quality is poor even before starting therapy. This used to be seen as a reason to not freeze sperm. In-vitro fertilization (IVF) has improved, and the use of intracytoplasmic sperm injection (ICSI) has been successful, even with limited number of sperm in a sample.

It is best to collect samples before starting therapy for cancer, but they can still be collected after therapy has started. If collection happens after therapy has started, men should be aware of the chance of the sperm having genetic damage. This damage and risk to the fetus has not been well studied, so there are no statistics on the chance of problems.

If a man is interested in freezing sperm, he will be sent to a fertility clinic to have the sperm collected in person. In some cases, a man can be provided with a collection kit to be done at home and mailed to the storage facility. Semen samples are best collected through masturbation after refraining from sexual activity for 2-5 days. More samples can be collected, with at least 48 hours between samples. This will provide an optimal number of sperm. Men without enough sperm in their semen can have
sperm removed from the testicle with a needle (called aspiration).

The samples are mixed with a substance to protect them from the freezing and thawing process. They are slowly frozen to the right temperature and stored. When the samples are needed, they are slowly thawed to protect the sperm from damage. It is not known exactly how long sperm can survive the freezing process, but it is thought to be many years.

The cost of collection, freezing, and storage varies greatly and it may be worth a few phone calls to find the best pricing. There are fees to store the samples, which can be charged monthly, yearly, or for a period of 1-5 years paid in advance. In some cases, insurance may cover these fees, so check with the insurance company. There are also costs tied to IVF to consider, which is necessary to use the sperm later.

Other Preservation Techniques Being Studied

While sperm banking is a good choice for many, there are men who cannot put-off treatment by a few days to bank sperm. In addition, boys treated before puberty do not yet produce sperm and cannot bank. There are a few techniques being studied, but unfortunately, they are still in the research stage.

Testicular Tissue Freezing

In this procedure, testicular tissue is removed and frozen, before cancer therapy starts. This tissue would be thawed for use at a later date. There are a few ways this tissue may be used:

- Sperm stem cells are collected from the tissue and implanted back into the man's testicles. The hope is that these cells begin to produce sperm and a man can impregnate a female normally.
- The tissue can be implanted in the man - either in the testicle or elsewhere. After the tissue begins making sperm, it is collected using a needle. This sperm is then used through IVF procedures to result in pregnancy.

This technique has been successful in animals, but there have been no live human births yet. Many fertility clinics use this technique, but men should know that this is purely experimental at this time.

Gonadoprotection

One other method that has been tested is called gonadoprotection. This works on the theory that germ cells are harmed by chemotherapy because they are quickly dividing and reproducing. By giving medication to stunt the reproduction of these cells, perhaps they would be safe from the damage of chemotherapy. This did not prove true when tested in humans and sperm production did not get better after therapy in the men studied.

The Future

While sperm cryopreservation is a sound choice for many men, it leaves out the many childhood cancer survivors from the dream of starting a biologic family. Future research will hopefully find methods to preserve fertility in these young men. Testicular tissue cryopreservation holds great hope and will be a focus in the years to come.