

Testicular and Reproductive Health after Cancer Treatment

The effects of childhood cancer therapy on reproductive function depend on many factors, including the specific type and location of the cancer, and the treatment that was given. It is important to understand how the testes function and how they may be affected by cancer treatment.

The reproductive system

The reproductive system contains many structures and is controlled by the pituitary gland in the brain. The testes are located in the scrotum (the loose pouch of skin behind the penis). The testes are made up of leydig cells (cells that produce the hormone—testosterone) and sertoli cells (cells that support the sperm production). At the time of puberty, the pituitary gland in the brain releases two hormones (FSH and LH) that signal the testes to begin producing sperm and testosterone. As puberty progresses, testosterone causes deepening of the voice, enlargement of the penis and testes, growth of facial and body hair, and muscular development of the body.

How does cancer therapy affect the testes?

Cancer therapy can cause infertility (the inability to initiate a pregnancy). Infertility can occur following treatment with certain types of chemotherapy, radiation to the brain or testes, or surgery involving the reproductive system.

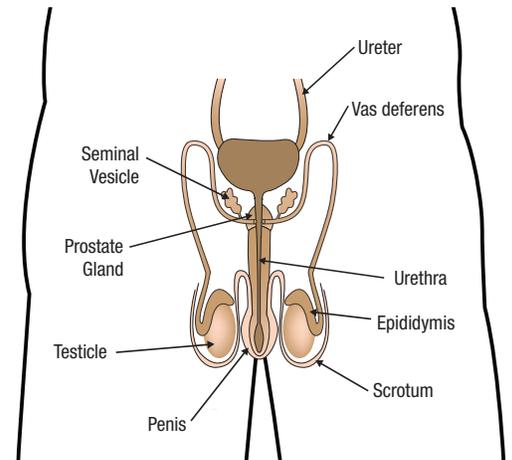
Another possible effect of cancer therapy is testosterone deficiency, also known as “hypogonadism”. When this occurs, the testes are unable to produce enough testosterone hormone. If this happens before the age of puberty, puberty may not start without hormone medication prescribed by a doctor. If it develops after puberty, testosterone therapy may be needed to maintain muscular development, bone and muscle strength, proper distribution of body fat, sex drive, and the ability to have erections.

What are the causes of male reproductive problems after childhood cancer treatment?

Chemotherapy of the “alkylator” type (such as cyclophosphamide, thiotepa, melphalan and busulfan) and heavy metals (such as cisplatin and carboplatin) may cause testicular damage. The total dose of chemotherapy used during cancer treatment is important in determining the likelihood of damage. The higher the total dose, the more potential for developing problems such as infertility or testosterone deficiency. If alkylating or heavy metal chemotherapy was used in combination with radiation, the risk for testicular damage is increased.

Radiation therapy can affect testicular function in two ways:

- **Radiation aimed directly at or near the testes.** The sperm-producing cells are very sensitive to the effects of radiation therapy. Most individuals who receive radiation to the testes at doses of 6 Gy (600 cGy/rads) or higher will be infertile. The testosterone producing cells are more resistant to the effects of radiation and chemotherapy, but if testicular radiation was given in doses of 12 Gy (1200 cGy/rads) or higher, the leydig cells may be damaged, resulting in testosterone deficiency (in addition to infertility).
- **Radiation to the hypothalamic and pituitary gland regions in the brain.** The hypothalamus and pituitary gland regulate the production of two hormones (LH and FSH) needed to signal the testes to make testosterone and sperm. People with low levels of these hormones will need to take testosterone hormone replacement. For some



survivors, it is possible to regain fertility with the use of specialized hormone treatments. Individuals who have infertility as a result of brain radiation and wish to achieve fertility should see a fertility specialist.

Surgery that involves removal of both testicles (bilateral orchiectomy) will result in infertility and testosterone deficiency. Pelvic surgery, such as retroperitoneal lymph node dissection (RPLD), or spinal surgery sometimes results in nerve damage that may prevent the ejaculation of sperm. Removal of the prostate or bladder may result in difficulties achieving an erection and/or ejaculation. In these situations, sperm production may be unaffected and fertility may still be possible by using specialized techniques, such as sperm harvesting and artificial insemination. If fertility is desired, consultation with a fertility specialist is recommended.

What types of cancer therapy increase the risk of problems with testicular function?

- **Chemotherapy** - the class of drugs called “alkylators” can cause infertility when given in high doses. Very high doses may occasionally cause testosterone deficiency. Heavy metal chemotherapy can also affect testicular function. Examples of these drugs are:

Alkylating agents:

- Busulfan
- Carmustine (BCNU)
- Chlorambucil
- Cyclophosphamide (Cytoxan®)
- Ifosfamide
- Lomustine (CCNU)
- Mechlorethamine (nitrogen mustard)
- Melphalan
- Procarbazine
- Thiotepa

Heavy metals:

- Carboplatin
- Cisplatin

Non-classical alkylators:

- Dacarbazine (DTIC)
- Temozolomide

- **Radiation therapy** to any of the following areas may cause infertility:
 - Testes
 - Total body irradiation (TBI)
 - Head/brain especially if dose was 30 Gy (3000 cGy/rads) or higher

In addition to causing infertility, high doses of radiation to the testes (usually 12 Gy or higher) or brain (usually 30 Gy or higher) may also cause testosterone deficiency.

- **Surgeries** that may cause infertility or disrupt normal sexual functioning include:
 - Removal of both testicles (this surgery will always result in infertility)
 - Removal of one testicle or a portion of one testicle
 - Retroperitoneal lymph node dissection (RPLD)
 - Removal of tumor in the retroperitoneal area
 - Pelvic surgery
 - Cystectomy (removal of the bladder)
 - Prostatectomy (removal of the prostate)

- Spinal surgery
- Removal of tumor near the spinal cord

In addition, removal of both testicles will result in testosterone deficiency, and removal of one testicle or a portion of one testicle may result in low testosterone levels.

What monitoring is recommended?

Individuals whose treatment places them at risk for problems with the reproductive system should have a yearly check-up that includes careful evaluation of their sexual development. Blood may be tested for hormone levels (AM testosterone, LH, FSH, and inhibin). If any problems are detected, a referral to an endocrinologist (hormone specialist), urologist (specialist in the reproductive system) and/or fertility specialist may be recommended. Individuals who have had both testes removed should begin seeing an endocrinologist starting at about age 11 for hormone replacement.

People who have had fertility preservation procedures (saving sperm outside of the body or “cryopreserved”), should review previous fertility counseling and current options for family building with a fertility specialist.

What can be done for testosterone deficiency?

Individuals with low testosterone levels should receive testosterone replacement therapy. Testosterone is available in several forms, including skin patches, injections, and topical gel. Your endocrinologist will determine which form of therapy is best for you.

How will I know if I am infertile?

Infertility, the inability to initiate a pregnancy after a year of unprotected intercourse, can occur after cancer treatment. Recovery of the ability to make sperm may occur in some survivors. When recovery occurs, it usually happens in the first few years after completion of cancer treatment. The best way to assess the ability to make sperm is a semen analysis which evaluates the number of sperm produced, the motility (movement of the sperm) and morphology (what the sperm look like). The specimen is produced after several days of abstinence. If the patient is unable to produce a semen specimen or prefers not to, an FSH and inhibin level may provide some insight into the ability to make sperm. A high FSH or low inhibin suggest impaired ability to make sperm.

A semen analysis that shows azoospermia (no sperm in the semen sample) on more than one sample is an indicator of infertility. Patients with oligospermia (low sperm count) may still be able to have children with the help of fertility specialists.

In general, contraception should be used unless pregnancy is desired.

What if only one testicle or a portion of one testicle was surgically removed?

Although fertility and testosterone production are not usually affected if only one testicle or a portion of one testicle was surgically removed, you should take precautions to protect the remaining testicle from injury by always wearing an athletic supporter with a protective cup when participating in any activities that may potentially cause injury to the groin area (such as contact sports, baseball, etc.).

What are the risks if pregnancy occurs after childhood cancer treatment?

Fortunately, in most cases, there is no increased risk of cancer or birth defects in children born to childhood cancer survivors. In rare cases, if the type of cancer in childhood was a genetic (inherited) type, then there may be a risk of passing that type of cancer on to a child. You should check with your oncologist if you are not sure whether the type of cancer you had is associated with a genetic risk that can be passed on.

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Additional health information for childhood cancer survivors is available at
www.survivorshipguidelines.org

Note: Throughout this *Health Links* series, the term “childhood cancer” is used to designate pediatric cancers that may occur during childhood, adolescence, or young adulthood. Health Links are designed to provide health information for survivors of pediatric cancer, regardless of whether the cancer occurred during childhood, adolescence, or young adulthood.

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