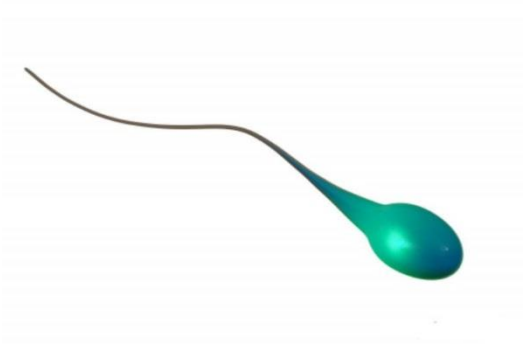
Cancer Association of South Africa (CANSA)

Research • Educate • Support

Fact Sheet on Testicular Cancer and Male Fertility

Introduction

Male infertility refers to a male's inability to cause pregnancy in a fertile female. In humans it accounts for 40-50% of infertility. Male infertility is commonly due to deficiencies in the semen, and semen quality is used as a surrogate measure of male fertility.



[Picture Credit: Sperm]

Individuals who learn they are infertile often experience the normal but nevertheless distressing emotions common to those who are grieving any significant loss — in this case the ability to procreate. Typical reactions include shock, grief, depression, anger, and frustration, as well as loss of self-esteem, self-confidence, and a sense of control over one's destiny.
(Wikipedia; Harvard Medical School).

The Male Reproductive System

The male reproductive tract is made up of the testes, a system of ducts (tubes) and other glands opening into the ducts.

The testes (testis: singular) are a pair of egg shaped glands that sit in the scrotum next to the base of the penis on the outside of the body. Each normal testis is 15 to 35ml in volume in adult men. The testes are needed for the male reproductive system to function normally.

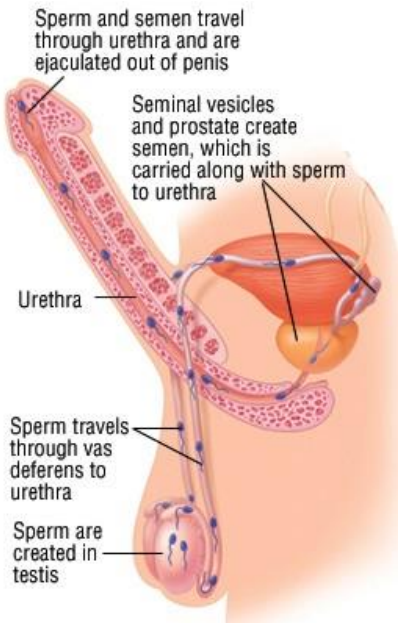
The testes have two related but separate roles:

- production of sperm
- production of the male sex hormone, testosterone.

Male infertility can be caused by problems that affect sperm production or the sperm transport process. With the results of medical tests, doctors are able to find the cause of the problem.

Sperm production problems: The most common cause of male infertility is due to a problem in the sperm production process in the testes. Low numbers of sperm are made and/or the sperm that are made do not function properly. About two thirds of infertile men have sperm production problems.

Blockage of sperm transport: Blockages (often referred to as obstructions) in the tubes leading sperm away from the testes to the penis can cause a complete lack of sperm in the ejaculated semen.



[Picture Credit: Fertility]

This is the second most common cause of male infertility and affects about one in every five infertile men, including men who have had a vasectomy but now wish to have more children.

Sperm antibodies: In some men, substances in the semen and/or blood called sperm antibodies can develop which can reduce sperm movement and block egg binding (where the sperm attaches to the egg) as is needed for fertilisation. About one in every 16 infertile men has sperm antibodies.

Sexual problems: Difficulties with sexual intercourse, such as erection or ejaculation problems, can also stop couples from becoming pregnant. Sexual problems are not a common cause of infertility.

Hormonal problems: Sometimes the pituitary gland does not send the right hormonal messages to the testes. This can cause both low testosterone levels and a failure of the testes to produce sperm.

Hormonal causes are uncommon, and affect less than one in 100 infertile men. Unfortunately, medical scientists do not yet understand all the details of sperm production and the fertilisation process. As a result, for many men with a sperm production problem, the cause cannot be identified.
(Andrology Australia).

Incidence of Testicular Cancer in South Africa

The following South African statistics regarding histologically diagnosed cases of testicular cancer during 2012 are available from the National Cancer Registry (2012):

Group 2012	Actual No of Cases	Percentage of All Cancers	Estimated Lifetime Risk
All males	170	0,21%	1:1 050
Asian males	12	1,45%	1:938
Black males	33	0,28%	1:7 123
Coloured males	17	0,40%	1:2 058
White males	108	0,54%	1:279

The frequency of histologically diagnosed cases of testicular cancer in South Africa for 2012 was as follows (National Cancer Registry, 2012):

Group 2012	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All males	12	48	59	36	9	2	3	1
Asian males	0	3	6	3	0	0	0	0
Black males	9	7	7	5	1	1	1	1
Coloured males	1	7	6	3	0	0	0	0
White males	2	30	38	25	8	1	2	0

Testicular Cancer and Infertility

Testicular cancer affects men mostly in their reproductive age. Fertility problems are usually complex and when testicular cancer is involved, they become even more complicated.

Testicular cancer and its treatment can affect hormone levels and might affect a man's ability to father children after treatment. It is, therefore, important to discuss the possible effects with a doctor before starting testicular cancer treatment so that one is aware of the risks and what options may be available.

Most boys and men who develop testicular cancer, develop cancer in only one testicle. The remaining testicle usually can make enough testosterone (the main male hormone) to keep the person healthy. If the other testicle needs to be removed because the cancer is in both testicles, or if a new cancer develops in the other testicle, the individual will need to take some form of testosterone for the rest of his life. Most often this is in the form of a gel or patch that is applied to the skin or a monthly injection.

Testicular cancer or its treatment can make a person infertile (unable to father a child). Before treatment starts, men who might wish to father children later on, may want to consider storing sperm in a sperm bank for later use. Infertility can be an issue later in life for boys who had testicular cancer. If a boy has already gone through puberty, sperm banking is often a good option, since the frozen samples are not damaged by long periods of storage. Researchers are currently looking at new techniques that might allow younger boys to someday father children.
(American Cancer Society; The Testicular Cancer Resource Center; Matos, Skrbinc & Zakotnik, 2010).

Surgery for Testicular Cancer and Fertility

Removing a testicle will not affect a person's sexual performance or his ability to father children. The healthy testicle (unless it is very small) will produce more testosterone and sperm to make up for the testicle that has been removed.

Men who have an operation to also remove the retroperitoneal lymph nodes may get nerve damage, which will cause retrograde ejaculation, meaning that sperm goes backwards during ejaculation into the bladder instead of coming out through the tip of the penis. The sperm is then passed out harmlessly in the urine. This type of surgery does not stop a person from getting an erection or having sex, but the orgasm will feel different because it is 'dry' (a dry climax).

New surgical techniques mean that this problem can be avoided. It is important, however, to speak to the treating specialist beforehand for advice about storing sperm.
(MacMillan Cancer Support).

Radiation Therapy for Testicular Cancer and Fertility
Radiation therapy can cause infertility in two distinct ways:

Primary testicular damage - occurs from radiation aimed directly at or near the testicles. Spermatogonia (sperm forming) cells are extremely sensitive to the effects of radiation therapy. Doses as low as 600 cGy can cause irreversible damage to the sperm forming cells. Doses less than this may cause a temporary drop in the number and quality of sperm produced.

The type and dimensions of cancer determine the area of the body to be radiated and how much radiation will be given. For example, radiation may be delivered directly to the testicles, as is used for treatment of testicular leukaemia and as part of the total body irradiation used in bone marrow transplant.

Testicular leukaemia - one to two percent of boys have leukaemia cells in the testicles at the time of their leukaemia diagnosis. This is determined by examining the testicles; in some cases a biopsy may be required. Stronger treatment is usually given to boys that have leukaemia in the testicles, and some will need to get radiation therapy (Cure Search for Children's Cancers).

Scatter radiation is the term used to describe radiation that occurs in areas not directly within the radiation therapy treatment field, but near to it. Examples of radiation sites that may result in scatter radiation to the testis include: radiation to the lymph nodes in the lower abdomen used for treatment of higher stage Hodgkin's Lymphoma or testicular cancer, or radiation delivered to the upper thigh for a tumour located in this area. Lead shields are used to protect the testis when the treatment field is nearby, but small amounts of radiation exposure may still occur.

Leydig cells are relatively resistant to the damaging effects of radiation therapy. Normal function remains following exposure or treatment with doses less than 2400cGy. This is important because Leydig cells produce testosterone, which is required for normal sexual development and normal sexual activity.

Secondary or indirect testicular failure - may occur following radiation therapy to the brain. Radiation may damage the pituitary gland, located in the brain, which is responsible for secreting hormones needed for normal sexual function. Pituitary damage may result in low doses of the hormones (FSH and LH) needed to stimulate the sperm forming cells and Leydig cells. Both LH and FSH are produced in the brain by the pituitary gland. High levels of radiation to the brain can damage the pituitary gland, resulting in an inability to produce the hormones FSH or LH. This in turn causes infertility and low testosterone levels.
(Comprehensive Cancer Center).

Chemotherapy for Testicular Cancer and Infertility
Not all chemotherapy drugs affect fertility in men. But some can. It may affect male fertility:

- By reducing the number of sperm produced
- By affecting the sperm's ability to fertilise an egg

If this happens it may be temporary or permanent and, if permanent, means that the individual will no longer be able to father children. Whether it is temporary or permanent depends on the drugs used, the doses administered and the age of the patient. Permanent infertility is more likely if higher doses of the drugs are administered.

It is important to use contraception throughout treatment. It is not advisable to father a child while receiving chemotherapy – the drugs could harm the baby.

Some chemotherapy drugs can affect the nerves in the genital area. This can temporarily make it difficult to get or maintain an erection. This usually gradually gets better once the treatment is finished. Usually one can still get an erection and have an orgasm as before. Chemotherapy drugs do not normally have any permanent effect on sexual performance or enjoyment of sex (Cancer Research UK).

It is extremely difficult to predict which men will become infertile as a result of chemotherapy treatments. The effects are dependent on the type and number of chemotherapy drugs received, as well as the cumulative dose received. The group of chemotherapies called alkalating agents are known to be the biggest offenders, but this varies based on the dose received. The following table addresses some common doses of chemotherapies and the likelihood of azoospermia (absence of motile, and hence viable, sperm in the semen). It is estimated that 90% of patients who receive high doses of alkalating agents will have long-term azoospermia. For those patients who have undergone stem cell transplants, 50% will have azoospermia, while the rates are as high as 80% for those who received total body irradiation (TBI) in preparation for the transplant

Table of chemotherapy drugs that may affect male fertility:

Chemotherapy Agent (Dose to cause effect)	**Known Effect on Sperm Count**
Chlorambucil (1.4g/m2) Cyclophosphamide (19g/m2) Procarbazine (4g/m2) Melphalan (140mg/m2) Cisplatin (500mg/m2)	Prolonged or permanent azoospermia
BCNU (1g/m2) CCNU (500mg/m2)	Azoospermia in adulthood if treated before puberty
Busulfan (600mg/m2) Ifosfamide (42g/m2) BCNU (300mg/m2) Nitrogen mustard Actinomycin D	Azoospermia likely, and are often given with other highly sterilising agents, adding to the effect
Doxorubicin (770mg/m2) Thiotepa (400mg/m2) Cytarabine (1g/m2) Vinblastine (50g/m2) Vincristine (8h/m2)	When used alone, cause only temporary reductions in sperm count. In conjunction with above agents, may be additive in causing azoospermia
Amsacrine Bleomycin Dacarbazine Daunorubicin Epirubicin Etoposide Fludarabine Fluorouracil 6-mercapatouprine Methotrexate Mitoxantrone Thioguanine	When used in conventional regimens, cause only temporary reductions in sperm count. In conjunction with above agents, may be additive in causing azoospermia

To complicate matters further, in many cases, azoospermia (no sperm) or oligospermia (low sperm count) is temporary, with sperm production recovering in the months to as long as 4 years following therapy. Sperm counts do appear to be lower after chemotherapy, and there can be damage to the genetic makeup (DNA) of sperm after chemotherapy. Research has found that this damage is repaired by two years after therapy, although the exact time to repair is not known. For this reason, men are typically counselled to wait two years after therapy before fathering a child (Oncolink).

Lowering the Risk of Testicular Cancer Coming Back

Many individuals ask whether there are specific lifestyle changes they can make to reduce their risk of testicular cancer coming back. Unfortunately, for most cancers there is little solid evidence to guide people. This does not mean that nothing will help – it is just that for the most part this is an area that has not been well studied. Not enough is known about testicular cancer to say for sure if there are things one can do that will be helpful.

Adopting healthy behaviours such as not smoking, eating well, being active, and staying at a healthy weight may help, but no one knows for use.

Sperm Banking – Semen Cryopreservation

Sperm banking (semen cryopreservation) involves harvesting and then freezing sperm at very low temperatures around minus 196^{o}C (a home freezer will not work!). Men may choose to bank sperm if there is a possibility of losing fertility. This is an important option for men who have not established a family or whose family is not yet complete.

Assisted reproduction techniques are medical procedures that help infertile couples achieve pregnancy. Using these methods, pregnancy can occur using frozen semen samples that have very low numbers of sperm. For this reason, all men who hope to father a child in the future should consider cryopreservation of semen or testicular tissue, even if the specimens have low numbers of sperm.

When the time is right, one's female partner can undergo artificial insemination to conceive a baby. Frozen sperm can last decades, if not longer.

If the affected young man is under the age of 18, it may be up to his parents to start the conversation about sperm banking.
(Everyday Health; Comprehensive Cancer Center).

Reasons Why Men Should Consider Semen Cryopreservation

- Before undergoing cancer therapies – therapies such as surgery, chemotherapy and radiation can cause permanent sterility and infertility
- Before have prostate or testicular surgery – damage can be caused to a man's reproductive organs during testicular surgery and prostatectomy
- Before having a vasectomy – to preserve fertility and prevent the need for reversal surgery if personal circumstances change
- High risk occupations – men exposed to chemical, radiation, extreme heat, etc can lead to infertility

- When men are going to be absent – semen freezing enables the female partner to continue with her reproductive schedule even if the male partner cannot be there due to work commitments or unforeseen circumstances
- Professional sportsmen (especially cyclists) – strenuous and consistent impact can lead to infertility

(Netcells Biosciences).

In a recent study by Quinn, *et al*. (2014) they found that out of a total of 231 records of adolescent and young adult men, in only 13% of cases was there any evidence of referral to a fertility specialist. They concluded that there is a need to create interventions to improve this.

Sperm Banking (Semen Cryopreservation) in South Africa

In South Africa sperm banking (semen cryopreservation) can be arranged through:

Vitalab Centre for Assisted Conception
Tel 0861 882522
http://www.vitalab.com/treatment-programs/sperm-freezing/

NetCells Biosciences
Tel: 0861 NETCELLS
https://www.netcells.co.za/reproductive-sperm.php?gclid=CIuTr9e3zMECFVHMtAodNFkArQ

Androcryos
Tell: 011 484 2695
http://androcryos.co.za/lab/contact-us.html

Cape Cryobank
Tell: 021 674 2088
http://capecryobank.co.za/

Your Parenting
http://www.yourparenting.co.za/fertility/treatment-options/sperm-banking-for-life

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