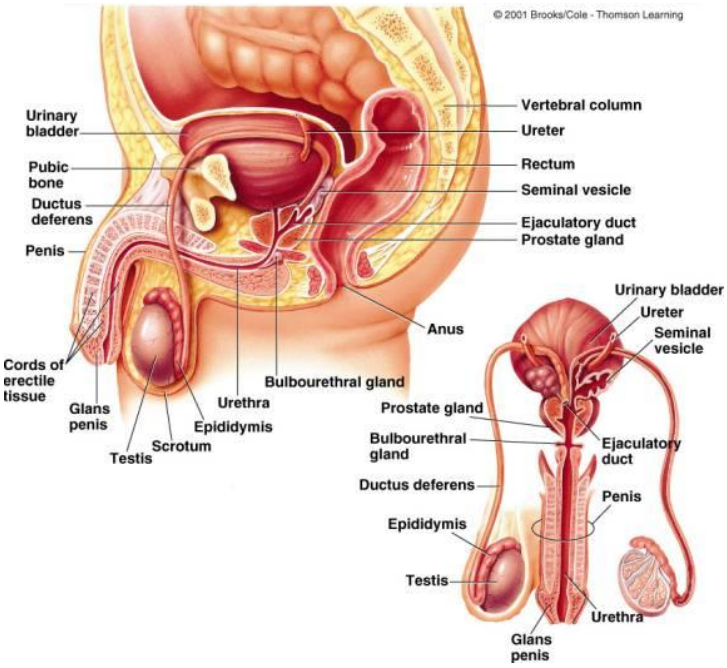
Cancer Association of South Africa (CANSA)

Research • Educate • Support

Fact Sheet on Testicular Cancer

Introduction

The testicles are two oval glands situated in the scrotum (sac) and are the male sexual organs that produce male sex hormones and sperm. They form part of the male reproductive system. The epididymis is a soft tubular structure behind each testicle which collects, stores and carries sperm. It connects with the *vas deferens* that joins the urethra in the prostate gland. The *Sertoli Cells* (germ cells) produce sperm while the *Leydig Cells* produce the male sex hormone *testosterone* (Diagram credit: WebMD).



[Picture Credit: Male Reproductive System]

Testicular cancer is a disease in which cells in one or both testicles become malignant (cancerous). It is not contagious and cannot spread from one person to another. This form of cancer is relatively rare when compared with other types of cancer. Testicular cancer accounts for approximately 1 percent of all cancers in men. However, it is the most common male cancer in men between the ages of 15 and 39 (National Cancer Institute; Mayo Clinic).

Testicular Cancer

Testicular cancer arises mostly (98,9%) in the germ cells of the testes in adults. Non-germ cell testicular tumours are uncommon and comprise a heterogeneous group.

Within the germ cell neoplasms tumours can be classified, based on pathologic and clinical features, into two broad histologic groups: seminomas and non-seminomas. Seminomas tend to

grow more slowly and are very sensitive to radiation therapy, compared to non-seminomas which are more clinically aggressive and do not respond well to radiotherapy, Because these two types of cancers grow and spread differently, they are treated differently (SEER Survival Monograph; National Cancer Institute).

Incidence of Testicular Cancer in South Africa

The following South African statistics regarding histologically diagnosed cases of testicular cancer during 2013 are available from the National Cancer Registry (2013):

Group 2013	Actual No of Cases	Percentage of All Cancers	Estimated Lifetime Risk
All males	156	0,43%	1:2 084
Asian males	14	1,72%	1:727
Black males	29	0,27%	1:7 613
Coloured males	18	0,44%	1:1 954
White males	95	0,47%	1:322

The frequency of histologically diagnosed cases of testicular cancer in South Africa for 2013 was as follows (National Cancer Registry, 2013):

Group 2013	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	17	41	38	37	13	6	2	0
Asian males	0	7	3	2	1	1	0	0
Black males	8	4	4	7	2	2	0	0
Coloured males	2	6	4	6	0	0	0	0
White males	6	24	27	21	9	3	2	0

Causes of Testicular Cancer

The exact cause of testicular cancer is unknown. We do, however, know that there are several risk factors linked to testicular cancer.

A risk factor is something that affects a person's chance of getting a particular disease. Different cancers have different risk factors. Some risk factors, such as smoking, can be controlled. Others, like a person's age or race, cannot be changed. However, having a risk factor, or even several risk factors, does not mean that a person will get the disease. Not having any risk factors does also not mean that someone will not get the disease (American Cancer Society).

Risk Factors for Testicular Cancer

There is no way to prevent testicular cancer (Mayo Clinic). Any person who believes that he may be at risk for testicular cancer should discuss this with his medical practitioner.
The following have been identified as risk factors for testicular cancer:

Having had an Undescended testicle(s) – before birth, the testicles normally develop in the belly of the foetus and then move down into the scrotum before the baby is born. It is estimated that in about 3% of boys, the testicles do not move down into the scrotum before birth (American Cancer Society). Sometimes the testicle stays inside the belly, while in other cases, it starts to move down, but gets stuck in the groin. Undescended testes is also known as *cryptorchidism*.

Men who have had *cryptorchidism* are several times more likely to get testicular cancer than those who did not have the problem. The risk is higher for men with a testicle in the belly as opposed to one that has moved down at least part of the way. Among men with a history of this problem, most cancers start in the testicle that has not moved down (National Cancer Institute).

Having had abnormal development of the testicles and/or other organs - men born with abnormalities of the testicles, penis and/or urethra (hypospadias), or kidneys, as well as those with inguinal hernia (hernia in the groin area, where the thigh meets the abdomen), may be at increased risk (CancerHelp UK).

Having a personal history of testicular cancer – Men who have been cured of cancer of one testicle have an increased risk (about 3-4%) of getting cancer in the other testicle (American Cancer Society).

Having a family history of testicular cancer - A family history of testicular cancer increases the risk. If a man has the disease, there is a slight increased risk that his brothers or sons may also get it. Approximately 10% of testicular cancers appear to be genetically linked. It is believed that the genes do not cause testicular cancer, but rather make the man more susceptible to it. (National Cancer Institute; Mark Kantrowitz).

HIV Infection – Recent research has shown that there is some evidence that men infected with HIV (human immunodeficiency virus) have an increased risk of testicular cancer. This may be especially true for men who have Aids (Acquired Immunodeficiency Syndrome). No other infections have been shown to increase testicular cancer risk (American Cancer Society).

Race – being white increases the risk of testicular cancer. White men are about 5 times more likely to get testicular cancer. The reason for this difference is not known (American Cancer Society; National Cancer Institute). Please also refer to the statistics from the National Cancer Registry quoted above.

Age – On average 9 out of 10 cases of testicular cancers occur in men between the ages of 20 and 54. However, this cancer can affect males of any age, including infants and older men (American Cancer Society).

Having fertility problems – studies have confirmed that men with fertility problems have an increased risk of testicular cancer. The problems they identified were low semen concentration, sperm that did not move around as much as normal, or a high proportion of abnormal sperm (CancerHelp UK).

Occupation - Certain occupations (miners, oil or gas workers, janitors, leather workers, food and beverage workers, or workers involved in the manufacturing or application of pesticides) have an increased risk of testicular cancer (Mark Kantrowitz).

Having a family history of breast cancer or malignant melanoma - men who have family members with breast cancer or malignant melanoma have an increased risk of testicular cancer (CancerHelp UK).

Smoking marijuana – Studies from the University of Chicago have found that men who had smoked marijuana were twice as likely as men who had not to get an aggressive form of the disease.

Body size – Some studies have shown that the risk of testicular cancer in somewhat higher in tall men, but other studies have not shown a link (American Cancer Society).

Having had a vasectomy - having had a vasectomy does not increase the risk of testicular cancer (West).

Having prior trauma to the testicles - Prior trauma to the testicles and recurrent actions such as horseback riding do not appear to be related to the development of testicular cancer.

Genetic risk factors - A new study looking at the genomes of more than 13 000 men identified four new genetic variants associated with an increased risk of testicular cancer, one of the commonly diagnosed type in young men today. The findings from this first-of-its-kind meta-analysis were reported online May 12 in *Nature Genetics* by researchers at the Perelman School of Medicine at the University of Pennsylvania.
(Web MD; American Cancer Society; Mayo Clinic; Medicalexpress.com; Cancer.net).

Testicular Cancer Survival Rates

The survival statistics quoted here come from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) database, and are based on patients who were diagnosed in the United States of America with testicular cancer between 1999 and 2007.

Localised testicular cancer	-	5-year relative survival rate* of 99% 10-year relative survival rate of 96%
Regional spread testicular cancer	-	5-year relative survival rate* of 96%
Distant spread testicular cancer	-	5-year relative survival rate* of 72%

[***** The 5-year relative survival rate refers to the percentage of patients who live at least 5 years after being diagnosed with cancer. Many of these patients live much longer than 5 years after diagnosis. The rates quoted above takes into account the fact that some patients with cancer will die from other causes and compare the observed survival with what would be expected for people without the cancer. This is seen to be a better way to see the impact of the cancer on survival.]

Signs and Symptoms of Testicular Problems

Like any other part of the boy, the testicles can be affected by various conditions and diseases, which can lead to symptoms. The most common signs and symptoms in the testicles and scrotum include:

- Lumps (masses)
- Swelling
- Pain

Cancer is only one of the possible causes of testicular symptoms. More often the symptoms are caused by injury, infection, or something else.

One cannot be sure as to whether a person has testicular cancer based on the presence of symptoms alone. It is, therefore, important that a medical practitioner is consulted in cases where symptoms become obvious.

The symptoms of testicular cancer include:

- Uncomfortable feeling in a testicle
- Presence of a painless lump on a testicle – the lump can sometimes be as small as a grain of rice and feel like hard rubber
- An enlarged or swollen testicle
- Significant shrinking of a testicle
- A change in the consistency of a testicle
- A heavy or aching feeling in the back, lower abdomen, groin, or scrotum
- Any painless lump on a testicle that does not respond promptly to antibiotic treatment
- If the cancer has already spread to the lungs, problems like shortness of breath, chest pain, or cough (even coughing up blood) may develop
- In rare cases, testicular cancer spreads to the brain and can cause headaches and confusion
- Enlargement of breasts with tenderness in cases of testicular germ cell tumours
- In Leydig cell tumours, oestrogen-producing tumours can cause loss of sexual desire or make the male's breasts to grow
- Also in Leydig cell tumours, androgen-producing tumours can cause growth of facial and body hair at an abnormally early age in boys
  (American Cancer Society; Testicular Cancer Symptoms).

Diagnosis of Testicular Cancer

The diagnosis of testicular cancer is done on the presence of symptoms followed by a physical examination and laboratory and diagnostic tests. These tests include:

- Blood tests that measure the levels of tumour markers like alpha-fetoprotein (AFP), beta-human chorionic gonadotropin (βHCG), and lactate dehydrogenase (LDH)
- Ultrasound – a test in which high-frequency sound waves are bounced off the testicles. The echoes produce a picture called a sonogram which can show the presence and size of a mass in the testicle
- Biopsy (microscopic examination of testicular tissue by pathologist) to determine whether cancer is present
- If testicular cancer is found, more tests are needed to find out if the cancer has spread from the testicle to other parts of the body. Determining the stage of the cancer helps the planning of appropriate treatment

Staging of Testicular Cancer

Once testicular cancer has been diagnosed, the doctor will perform more tests to determine whether the cancer has spread from the testicle to other parts of the body. Classifying a person's cancer by the degree to which it has spread is called staging. Staging is used to determine the available treatment options. Keep in mind that staging is only as accurate as the information available, and the stage of a person's cancer can change as more information or more accurate information is gathered. There are two type of staging: Clinical and Pathological. Clinical staging uses radiological and physical clues to estimate the stage. Pathological staging uses stronger evidence like tissue samples and blood tests to determine the stage.

After the required testing has been done, the doctors can assign a stage to the cancer. Roughly speaking, here are the Stages used:

Stage I: Cancer is found only in the testicle. Removing the testicle alone should cure the patient, though many will choose some form of additional treatment just to be sure.

Stage II: Cancer has spread to the lymph nodes in the abdomen. Removing the testicle alone will not cure the patient, and more treatment is necessary.

Stage III: Cancer has spread to areas above the diaphragm such as the lungs, neck or brain. There may be also be cancer in parts of the body such as the bones or liver. In this situation, chemotherapy is absolutely required. Surgery may also be needed.

Stage IV: To the best of my knowledge, there is no such thing as Stage IV testicular cancer. However, it is possible that Stage IV may still be used in some places in Europe. Suffice to say that Stage IV is probably very similar to Stage III.

Recurrent: Recurrent disease means that the cancer has come back after it has been treated. It may recur in the same place or in another part of the body.

The TNM System of Staging Testicular Cancer

Primary tumour (T) - The extent of primary tumour is classified after radical orchiectomy.

- pTX: Primary tumour cannot be assessed (if no radical orchiectomy has been performed, TX is used.)
- pT0: No evidence of primary tumour (e.g., histologic scar in testis)
- pTis: Intratubular germ cell neoplasia (carcinoma in situ)
- pT1: Tumour limited to testis and epididymis without lymphatic/vascular invasion
- pT2: Tumour limited to testis and epididymis with vascular/lymphatic invasion, or tumour extending through the tunica albuginea with involvement of the tunica vaginalis
- pT3: Tumour invades the spermatic cord with or without vascular/lymphatic invasion
- pT4: Tumour invades the scrotum with or without vascular/lymphatic invasion

Regional lymph nodes (N)

- NX: Regional lymph nodes cannot be assessed
- N0: No regional lymph node metastasis
- N1: Metastasis in a single lymph node, 2 cm or less in greatest dimension
- N2: Metastasis in a single lymph node, more than 2 cm but not more than 5 cm in greatest dimension; or multiple lymph nodes, none more than 5 cm in greatest dimension
- N3: Metastasis in a lymph node more than 5 cm in greatest dimension

Distant metastasis (M)

- MX: Presence of distant metastasis cannot be assessed
- M0: No distant metastasis
- M1: Distant metastasis
- M1a: Non-regional nodal or pulmonary metastasis
- M1b: Distant metastasis other than to non-regional nodes and lungs

The AJCC Stage Groupings

The AJCC stage groupings are as follows:

Stage 0	**Stage I**	**Stage II**	**Stage III**
pTis, N0, M0, S0	pT1-4, N0, M0, SX	Any pT/Tx, N1-3, M0, SX	Any pT/Tx, Any N, M1, SX
	Stage IA	**Stage IIA**	**Stage IIIA**
	pT1, N0, M0, S0	Any pT/Tx, N1, M0, S0 Any pT/Tx, N1, M0, S1	Any pT/Tx, Any N, M1a, S0 Any pT/Tx, Any N, M1a, S1
	Stage IB	**Stage IIB**	**Stage IIIB**
	pT2, N0, M0, S0 pT3, N0, M0, S0 pT4, N0, M0, S0	Any pT/Tx, N2, M0, S0 Any pT/Tx, N2, M0, S1	Any pT/Tx, N1-3, M0, S2 Any pT/Tx, Any N, M1a, S2
	Stage IS	**Stage IIC**	**Stage IIIC**
	Any pT/Tx, N0, M0, S1-3	Any pT/Tx, N3, M0, S0 Any pT/Tx, N3, M0, S1	Any pT/Tx, N1-3, M0, S3 Any pT/Tx, Any N, M1a, S3 Any pT/Tx, Any N, M1b, Any S

- In addition to the clinical stage definitions, surgical stage may be designated based on the results of surgical removal and microscopic examination of tissue.

- **Stage I** - Stage I testicular cancer is limited to the testis. Invasion of the scrotal wall by tumor or interruption of the scrotal wall by previous surgery does not change the stage but does increase the risk of spread to the inguinal lymph nodes, and this must be considered in treatment and follow-up. Invasion of the epididymis tunica albuginea and/or the spermatic cord also does not change the stage but does

increase the risk of retroperitoneal nodal involvement and the risk of recurrence. This stage corresponds to AJCC stages I and II.

- **Stage II** - Stage II testicular cancer involves the testis and the retroperitoneal or para-aortic lymph nodes usually in the region of the kidney. Retroperitoneal involvement should be further characterized by the number of nodes involved and the size of involved nodes. The risk of recurrence is increased if more than 5 nodes are involved, if the size of 1 or more involved nodes is larger than 2 centimetres, or if there is extranodal fat involvement. Bulky stage II disease describes patients with extensive retroperitoneal nodes (>5 centimetres) who require primary chemotherapy and who have a less favourable prognosis. This stage corresponds to AJCC stages III and IV (no distant metastasis).

- **Stage III** - Stage III implies spread beyond the retroperitoneal nodes based on physical examination, x-rays, and/or blood tests. Stage III is subdivided into nonbulky stage III versus bulky stage III. In nonbulky stage III, metastases are limited to lymph nodes and lung with no mass larger than 2 centimetres in diameter. Bulky stage III includes extensive retroperitoneal nodal involvement, plus lung nodules or spread to other organs such as liver or brain. This stage corresponds to AJCC stage IV (distant metastasis).

(Testicular Cancer Resource Centre).

Cryopreservation of Semen

A diagnosis of testicular cancer is a situation where depositing of semen in a long-term storage bank is something that each patient should consider. Long-term storage of sperm offers options for future preservation of semen and peace of mind. Circumstances can change and the affected person may want to father a child after treatment for his testicular cancer.

Cryopreservation of human spermatozoa - introduced in the 1960's - has been recognised as an efficient procedure for management of male fertility before therapy for malignant diseases, vasectomy or surgical infertility treatments, to store donor and partner spermatozoa before assisted reproduction treatments and to ensure the recovery of a small number of spermatozoa in severe male factor infertility.

[Picture Credit: Cryopreservation]

Sperm cryopreservation is an important component of fertility management and much of its successful application seems to affect the reproductive outcome of assisted reproduction technologies (ART): appropriate use of cryoprotectants before and sperm selection technologies after cryopreservation seem to have the greatest impact on preventing DNA fragmentation, thus improving sperm cryosurvival rates.

The procedure that makes it possible to stabilise the cells at cryogenic temperatures is called cryopreservation, also known as an applied aspect of cryobiology or the study of life at low temperatures. Many advances in the cryopreservation technology have led to the development of methods that allow for low-temperature maintenance of a variety of cell types including male and female gametes, small multicellular organisms, and even more complex organisms such as embryos. Cryopreservation of human spermatozoa has overcome many space and time limitations and now forms integral part of assisted reproduction technologies (ARTs).

This technique becomes particularly important in cases of preservation of male fertility before radiotherapy or chemotherapy which may lead to testicular failure or ejaculatory dysfunction. In fact, semen cryostorage seems to be the only proven method that may offer these couples a chance of having children in the future: cancer therapy could in fact lead to damage, resulting in subfertility or sterility due to gonad removal or permanent damage to germ cells caused by adjuvant therapy. In particular, the risk associated to therapy depends on several factors: the age of the patient at the time of treatment, the dose, site, and type of treatment. Male gamete freezing is largely recommended to preserve fertility in subjects who - for one reason or another - are exposed to potentially toxic agents which may interfere with gametogenesis (Advances in Urology).

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 having 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 things like chemicals, radiation and extreme heat can experience infertility
- Professional sportsmen (especially cyclists) – strenuous and consistent impact from the sport may possibly lead to infertility

How semen is stored

The semen is stored in small straws in liquid nitrogen in a cryogenic storage tank. Storage of 2-3 semen ejaculates is optimal, but this does depend on the volume of the ejaculate, the initial sperm count and forward progression of the sperm. The storage facility will analyse the sperm and will advise the client if more ejaculate is needed to be stored to ensure maximum reproductive success in the future.

Using cryogenically preserved semen for reproduction

Human semen has been cryogenically stored since the 1960's and due to ongoing research throughout the years, the process and techniques of cryopreservation have become more refined. In addition, birth defects among children 'conceived' using cryopreserved semen is no different to children 'conceived' using a fresh semen sample. However, there are concerns around this if the semen was produced after chemotherapy – this is why it is crucial to preserve fertility prior to cancer therapies. Many pregnancies are achieved with Artificial Reproductive

Technologies (ART) using cryogenically preserved semen samples but the success rate also depends on the female partner's fertility status and age.

Treatment of Testicular Cancer
The three types of standard treatment for testicular cancer are:

Surgery – to remove the affected testicle. This is usually done through an incision in the groin and is called a radical inguinal *orchidectomy*. This usually does not affect the man's ability to get an erection and to produce sperm (unless both testicles have been removed). For cosmetic purposes, a prosthesis (artificial testicle) can be placed in the scrotum at the time of the operation, or at any time afterward.

Radiation therapy – which is also referred to as radiotherapy. Use is made of high-energy rays to kill cancer cells and shrink tumours. Radiation therapy affects normal as well as cancerous cells. The side effects depend mainly on the treatment dose.

Chemotherapy – use is made of anticancer drugs to kill cancer cells. When chemotherapy is given to testicular cancer patients, it is usually given as adjuvant therapy (after surgery) to destroy cancerous cells that may remain in the body. Chemotherapy may also be the initial treatment if the cancer is advanced (has already spread outside the testicle).
(National Cancer Institute).

Follow-up Treatment
Regular follow-up treatment is very important as testicular cancer can recur and affect the remaining testicle. The person should consult his medical doctor for regular blood tests to measure tumour marker levels (National Cancer Institute).

Reducing the Risk for Testicular Cancer
There is no way to prevent testicular cancer. Unfortunately, testicular cancer is a type of cancer that can't easily be prevented. There are simply no proven prevention methods.

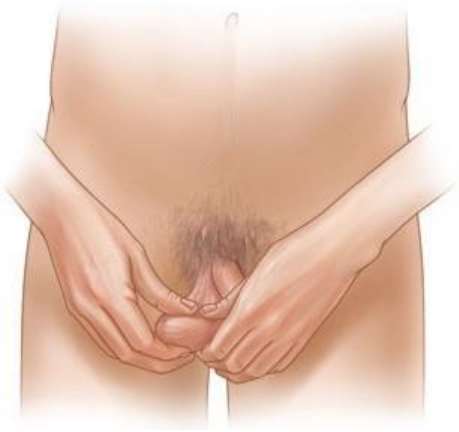
With most cancers, the best method of prevention is to avoid the risk factors and to do monthly testicular self-examinations. There is no way to avoid the risk factors for testicular cancer because most are out of the person's control, like age, race, and conditions occurring at birth. (Mayo Clinic; About.com).

Testicular Self Examination

The testicular self-examination (TSE) is an easy way for guys to check their own testicles to make sure there aren't any unusual lumps or bumps — which can be the first sign of testicular cancer.

Although testicular cancer is rare in teenage guys, overall it is the most common cancer in males between the ages of 15 and 39. It's important to try to do a TSE every month so you can become familiar with the normal size and shape of your testicles, making it easier to tell if something feels different or abnormal in the future.

[Picture Credit: RevolutionHealth]



Here is what to do:

- It's best to do a TSE during or right after a hot shower or bath. The scrotum (skin that covers the testicles) is most relaxed then, which makes it easier to examine the testicles
- Examine one testicle at a time. Use both hands to gently roll each testicle (with slight pressure) between your fingers. Place your thumbs over the top of your testicle, with the index and middle fingers of each hand behind the testicle, and then roll it between your fingers
- You should be able to feel the epididymis (the sperm-carrying tube), which feels soft, rope-like, and slightly tender to pressure, and is located at the top of the back part of each testicle. This is a normal lump
- Remember that one testicle (usually the right one) is slightly larger than the other for most guys — this is also normal
- When examining each testicle, feel for any lumps or bumps along the front or sides. Lumps may be as small as a piece of rice or a pea
- If you notice any swelling, lumps, or changes in the size of a testicle, a change in the colour of the scrotum, or if you have any pain or achy areas in your groin, let your doctor know right away
- Lumps or swelling may not be cancer, but they should be checked by your doctor as soon as possible. Testicular cancer is almost always curable if it is caught and treated early (KidsHealth).

About Clinical Trials

Clinical trials are research studies that involve people. These studies test new ways to prevent, detect, diagnose, or treat diseases. People who take part in cancer clinical trials have an opportunity to contribute to scientists' knowledge about cancer and to help in the development of improved cancer treatments. They also receive state-of-the-art care from cancer experts.

<u>Types of Clinical Trials</u>

Cancer clinical trials differ according to their primary purpose. They include the following types:

Treatment - these trials test the effectiveness of new treatments or new ways of using current treatments in people who have cancer. The treatments tested may include new drugs or new combinations of currently used drugs, new surgery or radiation therapy techniques, and vaccines or other treatments that stimulate a person's immune system to fight cancer. Combinations of different treatment types may also be tested in these trials.

Prevention - these trials test new interventions that may lower the risk of developing certain types of cancer. Most cancer prevention trials involve healthy people who have not had cancer; however, they often only include people who have a higher than average risk of developing a specific type of cancer. Some cancer prevention trials involve people who have had cancer in the past; these trials test interventions that may help prevent the return (recurrence) of the original cancer or reduce the chance of developing a new type of cancer.

Screening - these trials test new ways of finding cancer early. When cancer is found early, it may be easier to treat and there may be a better chance of long-term survival. Cancer screening trials usually involve people who do not have any signs or symptoms of cancer. However, participation in these trials is often limited to people who have a higher than average risk of developing a certain type of cancer because they have a family history of that type of cancer or they have a history of exposure to cancer-causing substances (e.g., cigarette smoke).

Diagnostic - these trials study new tests or procedures that may help identify, or diagnose, cancer more accurately. Diagnostic trials usually involve people who have some signs or symptoms of cancer.

Quality of life or supportive care - these trials focus on the comfort and quality of life of cancer patients and cancer survivors. New ways to decrease the number or severity of side effects of cancer or its treatment are often studied in these trials. How a specific type of cancer or its treatment affects a person's everyday life may also be studied.

Where Clinical Trials are Conducted

Cancer clinical trials take place in cities and towns in doctors' offices, cancer centres and other medical centres, community hospitals and clinics. A single trial may take place at one or two specialised medical centres only or at hundreds of offices, hospitals, and centres.

Each clinical trial is managed by a research team that can include doctors, nurses, research assistants, data analysts, and other specialists. The research team works closely with other health professionals, including other doctors and nurses, laboratory technicians, pharmacists, dieticians, and social workers, to provide medical and supportive care to people who take part in a clinical trial.

Research Team

The research team closely monitors the health of people taking part in the clinical trial and gives them specific instructions when necessary. To ensure the reliability of the trial's results, it is important for the participants to follow the research team's instructions. The instructions may include keeping logs or answering questionnaires. The research team may also seek to contact the participants regularly after the trial ends to get updates on their health.

Clinical Trial Protocol

Every clinical trial has a protocol, or action plan, that describes what will be done in the trial, how the trial will be conducted, and why each part of the trial is necessary. The protocol also includes guidelines for who can and cannot participate in the trial. These guidelines, called eligibility criteria, describe the characteristics that all interested people must have before they can take part in the trial. Eligibility criteria can include age, sex, medical history, and current health status. Eligibility criteria for cancer treatment trials often include the type and stage of cancer, as well as the type(s) of cancer treatment already received.

Enrolling people who have similar characteristics helps ensure that the outcome of a trial is due to the intervention being tested and not to other factors. In this way, eligibility criteria help researchers obtain the most accurate and meaningful results possible.

National and International Regulations

National and international regulations and policies have been developed to help ensure that research involving people is conducted according to strict scientific and ethical principles. In these regulations and policies, people who participate in research are usually referred to as "human subjects."

Informed Consent

Informed consent is a process through which people learn the important facts about a clinical trial to help them decide whether or not to take part in it, and continue to learn new information about the trial that helps them decide whether or not to continue participating in it.

During the first part of the informed consent process, people are given detailed information about a trial, including information about the purpose of the trial, the tests and other procedures that will be required, and the possible benefits and harms of taking part in the trial. Besides talking with a doctor or nurse, potential trial participants are given a form, called an informed consent form, that provides information about the trial in writing. People who agree to take part in the trial are asked to sign the form. However, signing this form does not mean that a person must remain in the trial. Anyone can choose to leave a trial at any time—either before it starts or at any time during the trial or during the follow-up period. It is important for people who decide to leave a trial to get information from the research team about how to leave the trial safely.

The informed consent process continues throughout a trial. If new benefits, risks, or side effects are discovered during the course of a trial, the researchers must inform the participants so they can decide whether or not they want to continue to take part in the trial. In some cases, participants who want to continue to take part in a trial may be asked to sign a new informed consent form.

New interventions are often studied in a stepwise fashion, with each step representing a different "phase" in the clinical research process. The following phases are used for cancer treatment trials:

Phases of a Clinical Trial

Phase 0. These trials represent the earliest step in testing new treatments in humans. In a phase 0 trial, a very small dose of a chemical or biologic agent is given to a small number of people (approximately 10-15) to gather preliminary information about how the agent is processed by the body (pharmacokinetics) and how the agent affects the body (pharmacodynamics). Because the agents are given in such small amounts, no information is obtained about their safety or effectiveness in treating cancer. Phase 0 trials are also called micro-dosing studies, exploratory Investigational New Drug (IND) trials, or early phase I trials. The people who take part in these trials usually have advanced disease, and no known, effective treatment options are available to them.

Phase I (also called phase 1). These trials are conducted mainly to evaluate the safety of chemical or biologic agents or other types of interventions (e.g., a new radiation therapy technique). They help determine the maximum dose that can be given safely (also known as the maximum tolerated dose) and whether an intervention causes harmful side effects. Phase I trials enrol small numbers of people (20 or more) who have advanced cancer that cannot be treated effectively with standard (usual) treatments or for which no standard treatment exists. Although evaluating the effectiveness of interventions is not a primary goal of these trials, doctors do look for evidence that the interventions might be useful as treatments.

Phase II (also called phase 2). These trials test the effectiveness of interventions in people who have a specific type of cancer or related cancers. They also continue to look at the safety of interventions. Phase II trials usually enrol fewer than 100 people but may include as many as 300. The people who participate in phase II trials may or may not have been treated previously with standard therapy for their type of cancer. If a person has been treated previously, their eligibility to participate in a specific trial may depend on the type and amount of prior treatment they received. Although phase II trials can give some indication of whether or not an intervention works, they are almost never designed to show whether an intervention is better than standard therapy.

Phase III (also called phase 3). These trials compare the effectiveness of a new intervention, or new use of an existing intervention, with the current standard of care (usual treatment) for a particular type of cancer. Phase III trials also examine how the side effects of the new intervention compare with those of the usual treatment. If the new intervention is more effective than the usual treatment and/or is easier to tolerate, it may become the new standard of care.

Phase III trials usually involve large groups of people (100 to several thousand), who are randomly assigned to one of two treatment groups, or “trial arms”: (1) a control group, in which everyone in the group receives usual treatment for their type of cancer, or 2) an investigational or experimental group, in which everyone in the group receives the new intervention or new use of an existing intervention. The trial participants are assigned to their individual groups by random assignment, or randomisation. Randomisation helps ensure that the groups have similar characteristics. This balance is necessary so the researchers can have confidence that any differences they observe in how the two groups respond to the treatments they receive are due to the treatments and not to other differences between the groups.

Randomisation is usually done by a computer program to ensure that human choices do not influence the assignment to groups. The trial participants cannot request to be in a particular group, and the researchers cannot influence how people are assigned to the groups. Usually, neither the participants nor their doctors know what treatment the participants are receiving.

People who participate in phase III trials may or may not have been treated previously. If they have been treated previously, their eligibility to participate in a specific trial may depend on the type and the amount of prior treatment they received.

In most cases, an intervention will move into phase III testing only after it has shown promise in phase I and phase II trials.

Phase IV (also called phase 4). These trials further evaluate the effectiveness and long-term safety of drugs or other interventions. They usually take place after a drug or intervention has been approved by the medicine regulatory office for standard use. Several hundred to several thousand people may take part in a phase IV trial. These trials are also known as post-marketing surveillance trials. They are generally sponsored by drug companies.

Sometimes clinical trial phases may be combined (e.g., phase I/II or phase II/III trials) to minimize the risks to participants and/or to allow faster development of a new intervention.

Although treatment trials are always assigned a phase, other clinical trials (e.g., screening, prevention, diagnostic, and quality-of-life trials) may not be labelled this way.

Use of Placebos

The use of placebos as comparison or “control” interventions in cancer treatment trials is rare. If a placebo is used by itself, it is because no standard treatment exists. In this case, a trial would compare the effects of a new treatment with the effects of a placebo. More often, however, placebos are given along with a standard treatment. For example, a trial might compare the effects of a standard treatment plus a new treatment with the effects of the same standard treatment plus a placebo.

Possible benefits of taking part in a clinical trial

The benefits of participating in a clinical trial include the following:

- Trial participants have access to promising new interventions that are generally not available outside of a clinical trial.
- The intervention being studied may be more effective than standard therapy. If it is more effective, trial participants may be the first to benefit from it.
- Trial participants receive regular and careful medical attention from a research team that includes doctors, nurses, and other health professionals.
- The results of the trial may help other people who need cancer treatment in the future.
- Trial participants are helping scientists learn more about cancer (e.g., how it grows, how it acts, and what influences its growth and spread).

Potential harms associated with taking part in a clinical trial
The potential harms of participating in a clinical trial include the following:

- The new intervention being studied may not be better than standard therapy, or it may have harmful side effects that doctors do not expect or that are worse than those associated with standard therapy.
- Trial participants may be required to make more visits to the doctor than they would if they were not in a clinical trial and/or may need to travel farther for those visits.

Correlative research studies, and how they are related to clinical trials
In addition to answering questions about the effectiveness of new interventions, clinical trials provide the opportunity for additional research. These additional research studies, called correlative or ancillary studies, may use blood, tumour, or other tissue specimens (also known as 'biospecimens') obtained from trial participants before, during, or after treatment. For example, the molecular characteristics of tumour specimens collected during a trial might be analysed to see if there is a relationship between the presence of a certain gene mutation or the amount of a specific protein and how trial participants responded to the treatment they received. Information obtained from these types of studies could lead to more accurate predictions about how individual patients will respond to certain cancer treatments, improved ways of finding cancer earlier, new methods of identifying people who have an increased risk of cancer, and new approaches to try to prevent cancer.

Clinical trial participants must give their permission before biospecimens obtained from them can be used for research purposes.

When a clinical trial is over
After a clinical trial is completed, the researchers look carefully at the data collected during the trial to understand the meaning of the findings and to plan further research. After a phase I or phase II trial, the researchers decide whether or not to move on to the next phase or stop testing the intervention because it was not safe or effective. When a phase III trial is completed, the researchers analyse the data to determine whether the results have medical importance and, if so, whether the tested intervention could become the new standard of care.

The results of clinical trials are often published in peer-reviewed scientific journals. Peer review is a process by which cancer research experts not associated with a trial review the study report before it is published to make sure that the data are sound, the data analysis was performed correctly, and the conclusions are appropriate. If the results are particularly important, they may be reported by the media and discussed at a scientific meeting and by patient advocacy groups before they are published in a journal. Once a new intervention has proven safe and effective in a clinical trial, it may become a new standard of care.
(National Cancer Institute).

Medical Disclaimer
This Fact Sheet is intended to provide general information only and, as such, should not be considered as a substitute for advice, medically or otherwise, covering any specific situation.

Users should seek appropriate advice before taking or refraining from taking any action in reliance on any information contained in this Fact Sheet. So far as permissible by law, the Cancer Association of South Africa (CANSA) does not accept any liability to any person (or his/her dependants/estate/heirs) relating to the use of any information contained in this Fact Sheet.

Whilst the Cancer Association of South Africa (CANSA) has taken every precaution in compiling this Fact Sheet, neither it, nor any contributor(s) to this Fact Sheet can be held responsible for any action (or the lack thereof) taken by any person or organisation wherever they shall be based, as a result, direct or otherwise, of information contained in, or accessed through, this Fact Sheet.

CANSA Support

The Cancer Association of South Africa (CANSA): www.cansa.org.za
Toll free line (08:00 to 16:30 on weekdays): 0800 22 66 22
E-mail: info@cansa.org.za

References and Consulted Sources:

About.com. Testicular Cancer Prevention.
http://cancer.about.com/od/testicularcancer/a/testiculoarprev.htm (Accessed on 2011-10-20).

Advances in Urology
http://www.hindawi.com/journals/au/2012/854837/

American Cancer Society. Testicular Cancer.
http://www.cancer.org/Cancer/TesticularCancer/MoreInformation/DoIHaveTesticularCancer/do-i-have-testicular-cancer-signs-of-problems (Accessed on 2011-10-19).
http://www.cancer.org/Cancer/TesticularCancer/DetailedGuide/testicular-cancer-survival-rates (Accessed on 2011-10-19).
http://www.cancer.org/Cancer/TesticularCancer/OverviewGuide/testicular-cancer-overview-what-causes (Accessed on 2011-01-19).
http://www.cancer.org/cancer/testicularcancer/detailedguide/testicular-cancer-risk-factors

CancerHelp UK. Testicular Cancer.
http://cancerhelp.cancerresearchuk.org/type/testicular-cancer/about/testicular-cancer-risks-and-causes (Accessed on 2011-10-19).

Cancer.net
http://www.cancer.net/cancer-types/testicular-cancer/risk-factors

Cryopreservation
https://www.google.co.za/search?q=cryopreservation+semen&source=lnms&tbm=isch&sa=X&ei=-6cpUsu1GOeh0QXa7ID4BA&ved=0CAcQ_AUoAQ&biw=1366&bih=614#facrc=_&imgdii=_&imgrc=quHdWr_peKKx8M%3A%3BzWhqmUIwfgCawM%3Bhttp%253A%252F%252Fwww.pushpaivf.com%252Fimages%252Fsperm-freezing.jpg%3Bhttp%253A%252F%252Fwww.pushpaivf.com%252Fsperm-freezing-and-banking.html%3B288%3B200

KidsHealth. Testicular Self Examination.
http://kidshealth.org/teen/sexual_health/guys/tse.html (Accessed on 2012-02-23).

Mark Kantrowitz. Testicular Cancer. http://www.kantrowitz.com/cancer/risk.html (Accessed on 2011-10-19).

Male Reproductive System
http://www.bing.com/images/search?q=free+pics+male+reproductive+system&view=detail&id=6ADFEE733B666EA4237F21204144DD6AB7202B9D&qpvt=free+pics+male+reproductive+system&FORM=IDFRIR

Mayo Clinic. Testicular Cancer.
http://www.mayoclinic.com/health/testicular-cancer/DS00046/DSECTION=prevention (Accessed on 2011-10-19).
http://www.mayoclinic.com/health/testicular-cancer/DS00046 (Accessed on 2011-10-19)
http://www.mayoclinic.com/health/testicular-cancer/DS00046/DSECTION=risk-factors

Medicalxpress
http://medicalxpress.com/news/2013-05-genetic-factors-testicular-cancer.html

National Cancer Registry. 2010. National Health Laboratory Services, National Department of Health.

National Cancer Institute. Testicular Cancer.
http://www.cancer.gov/cancertopics/factsheet/Sites-Types/testicular (Accessed on 2011-10-19).
http://www.cancer.gov/cancertopics/pdq/treatment/testicular/Patient (Accessed on 2011-10-19).
http://www.cancer.gov/clinicaltrials/learningabout/what-are-clinical-trials

RevolutionHealth. Diagram: Testicular Self Examination.
http://www.revolutionhealth.com/articles/testicular-self-examination-tse/zm6155 (Accessed on 2012-03-23).

Seer Survival Monograph. 2007. Ries, L.A.G., Young, J.L., Keel, G.E., Eisner, M.P., Lin, Y.D., Horner M-J. (Editors). SEER Survival Monograph: Cancer Survival Among Adults: U.S. SEER Program, 1988-2001, Patient and Tumor Characteristics. National Cancer Institute, SEER Program, NIH Pub. No. 07-6215, Bethesda, MD.

Testicular Cancer Resource Centre
http://tcrc.acor.org/staging.html

Testicular Cancer Symptoms.
http://testicular-cancer-symptoms.org/ (Accessed on 2011-10-19).

WebMD. Anatomical diagram male genitalia.
http://men.webmd.com/picture-of-the-penis (Accessed on 2012-03-23).
http://www.webmd.com/cancer/news/20120910/marijuana-tied-to-testicular-cancer

West, R.R. 1992. Vasectomy and testicular cancer: no association on current evidence. *British Medical Journal*, 304(6829): 729-730.