Cancer Association of South Africa (CANSA)

Research • Educate • Support

Fact Sheet
on
Cancer of the Pharynx
(Throat)

Introduction

In humans the pharynx (throat) is part of the digestive system and also of the conducting zone of the respiratory system. The conducting zone also includes the nose, larynx, trachea, bronchi and bronchioles, and their function is to filter, warm, and moisten air and conduct it into the lungs. It makes up the part of the throat situated immediately posterior (behind) to the nasal cavity, posterior to the mouth and superior (above) to the oesophagus and larynx. The human pharynx is conventionally divided into three sections: the nasopharynx, the oropharynx and the hypopharynx. It is also important in vocalisation.

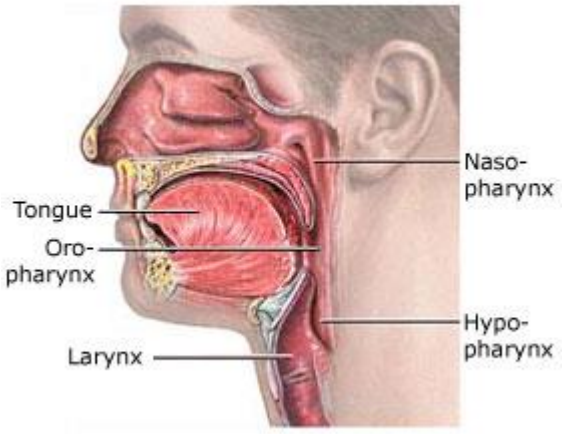
Cancer of the Pharynx

Pharyngeal cancer (also referred to as pharyngeal carcinoma) is cancer that occurs in the pharynx. The pharynx includes the space behind the nose and above the back of the throat.

It includes the following three parts:

- Nasopharynx
- Oropharynx
- Hypopharynx

[Picture Credit: Pharynx]



The nasopharynx connects the back of the nose to the back of the mouth. Cancer that develops in the nasopharynx is called nasopharyngeal cancer. One cannot see one's own nasopharynx directly, but by looking inside one's mouth in the mirror, it lies above the soft palate (the soft area at the back of the roof of the mouth) and uvula (the dangly bit) at the back of the mouth.

The other two parts of the pharynx are:

- The oropharynx – the part of the throat at the back of the mouth. Cancers that start in this area are oropharyngeal cancers.
- The hypopharynx (sometimes called the laryngopharynx) – it sits behind and on either side of the larynx (voice box). Cancer can also start in the hypopharynx.

(Cancer Research UK).

Researched and Authored by Prof Michael C Herbst
[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health]
Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

Incidence of Cancer of the Pharynx in South Africa
According to the National Cancer Registry (2012) the following number of cases of cancer of the naso-oropharynx was histologically diagnosed in South Africa during 2012:

Group - Males 2012	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All males	366	1:388	0,99%
Asian males	17	1:264	1,96%
Black males	188	1:500	1,61%
Coloured males	62	1:224	1,43%
White males	99	1:287	0,49%

Group - Females 2012	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All females	133	1:1 558	0,35%
Asian females	2	1:2 089	0,19%
Black females	69	1:2 412	0,42%
Coloured females	22	1:859	0,53%
White females	40	1:823	0,25%

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

Group - Males 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	8	10	14	48	92	135	40	12
Asian males	0	0	2	2	4	6	2	0
Black males	4	8	4	22	53	59	19	6
Coloured males	1	1	4	8	19	20	5	2
White males	0	0	3	7	27	20	9	3

Group - Females 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 females	5	9	12	19	30	34	15	9
Asian females	0	0	0	0	0	2	0	0
Black females	4	7	11	13	9	11	4	5
Coloured females	0	0	0	3	9	4	3	2
White females	0	2	1	2	8	16	7	2

N.B. In the event that the totals in any of the above tables do not tally, this may be the result of uncertainties as to the age, race or sex of the individual. The totals for 'all males' and 'all females', however, always reflect the correct totals.

Risk Factors for Pharyngeal Cancer
Risk factors for pharyngeal cancer include:

General Risk Factors:
- Lack of fruits and vegetables: A diet low in fruits and vegetables can increase the likelihood of developing throat cancer

Lifestyle Factors:
- Tobacco use: The use of cigarettes, pipes and cigars all increase the likelihood of developing pharyngeal cancer.
- Chewing tobacco or betel quid (gutkha)
- Alcohol use: Excessive use of alcohol can increase the risk for pharyngeal cancer

Other Factors:

- Human papillomavirus (HPV) Infection: New research has found that HPV infection is responsible for rising rates of pharyngeal cancer, in particular oropharyngeal cancer

- Gastro-oesophageal reflux disease (GERD): When acid leaks from the stomach into the oesophagus (food tube), it causes acid reflux. Chronic acid reflux is called GERD, and increases pharyngeal cancer risk depending on the frequency and severity of the acid reflux

- Contracting Epstein-barr virus (EBV): This common virus is transmitted via saliva. Contracting EBV increases the likelihood of developing pharyngeal cancer

- Low immunity - Research has found that people have an increased risk of mouth and throat cancer if they have a reduced immunity due to HIV or AIDS. Taking medicines to suppress immunity after organ transplants also gives a higher risk of mouth and throat cancer than in the general population.

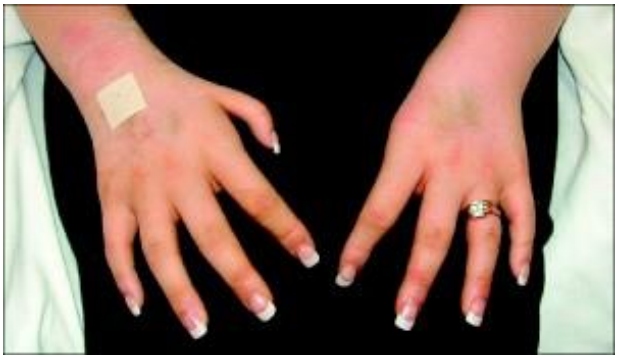
- Previous cancer - People who have had mouth or oropharyngeal cancer have an increased risk of getting a second one. Women have a higher risk of a second oral cancer than men.
  People who have had some other types of cancer also have an increased risk of mouth and throat cancer. These include
  - Cancer of the food pipe (oesophagus)
  - Squamous cell skin cancer
  - Cervical, anal or genital cancer in women
  - Cancer of the back passage (rectum) in men

- Family history - People often worry that they are at a higher risk of cancer because someone in their family has it. There does seem to be a slightly higher risk of getting mouth cancer if one has a close relative (a parent, brother, sister or child) who has had mouth cancer. The reason for this is unknown

- Mouth conditions - Sometimes changes can happen in the cells of the lining of the mouth and they cause red or white patches to appear. These changes are called leukoplakia and erythroplakia. In some people these changes may develop into cancer over some years. Dentists can see these changes during dental checks so it is important to have regular dental appointments to find these changes early.

- Genetic conditions - People with certain syndromes caused by inherited changes (mutations) in particular genes have a high risk of mouth and throat cancer. These include:

[Picture Credit: Fanconi Anaemia]



- Fanconi anaemia – a genetic disorder that can affect children and adults from any ethnic background. It is also called Fanconi's syndrome. People with Fanconi anaemia are short, have bone changes, and are at risk of developing cancers, leukaemia, and bone marrow failure (aplastic anaemia).

A common symptoms of Fanconi anaemia is abnormal hands.

- Dyskeratosis congenita – a genetic syndrome that can cause aplastic anaemia, skin rashes, and abnormally shaped fingernails and toenails. People with this syndrome have a high risk of developing cancer of the mouth and throat when they are young

(Cancer Treatment Centers of America; Cancer Research UK;

Signs and Symptoms of Pharyngeal Cancer

Signs and symptoms of pharyngeal cancer may include:

- A persistent cough
- Changes in your voice, such as hoarseness
- Difficulty swallowing
- Ear pain
- A lump or sore that does not heal
- Difficulty chewing, swallowing, or moving the jaw or tongue
- Changes in speech
- A persistent sore throat or a feeling that something is caught in the throat
- Unexplained weight loss
- Chronic bad breath
- Fatigue
- Loss of appetite, especially when prolonged: this may happen later in the course of the illness

An appointment should be made to see a doctor if any of the above signs and symptoms persist or any new signs and symptoms appear. Most pharyngeal cancer symptoms are not specific to cancer, so the doctor will likely investigate other more common causes first.
(Mayo Clinic; Cancer.Net; Macmillan Cancer Support).

Types of Pharyngeal Cancer

More than 9 out of 10 mouth and oropharyngeal cancers (90%) are squamous cell carcinoma. Squamous cells are the flat, skin like cells that cover the inside of the mouth, nose, larynx and throat. Carcinoma just means cancer. So squamous cell carcinoma is cancer that starts in these cells.

There is an unusual type of squamous cell carcinoma called verrucous carcinoma. About 1 in 20 mouth cancers (5%) are this type. Verrucous carcinoma rarely spreads to other parts of the body but can grow very deeply into surrounding tissues.

Though most throat cancers involve the same types of cells, specific terms are used to differentiate the part of the throat where cancer originated:

- Nasopharyngeal cancer begins in the nasopharynx - the part of the throat just behind the nose
- Oropharyngeal cancer begins in the oropharynx - the part of the throat right behind the mouth that includes the tonsils
- Hypopharyngeal cancer (laryngopharyngeal cancer) begins in the hypopharynx (laryngopharynx) - the lower part of the throat, just above the oesophagus and windpipe

- Glottic cancer begins in the vocal cords
- Supraglottic cancer begins in the upper portion of the larynx and includes cancer that affects the epiglottis, which is a piece of cartilage that blocks food from going into the windpipe
- Subglottic cancer begins in the lower portion of the voice box, below the vocal cords

(Cancer Research UK; Mayo Clinic).

Diagnosis of Pharyngeal Cancer

The following tests may be used to diagnose pharyngeal cancer:

- Physical examination - Dentists and doctors often find lip and oral cavity cancers during routine check-ups. If a person shows signs of oral or oropharyngeal cancer, the doctor will take a complete medical history, asking about the patient's symptoms and risk factors. The doctor will feel for any lumps on the neck, lips, gums, and cheeks. Since patients with oral or oropharyngeal cancer have a higher risk of other cancers elsewhere in the head and neck region, the area behind the nose, the larynx (voice box), and the lymph nodes of the neck are also examined.

- Endoscopy - This test allows the doctor to see inside the mouth and throat. Typically, an endoscope (a thin, flexible tube with an attached light and view lens) is inserted through the nose to examine the head and neck areas. Sometimes, a rigid endoscope (a hollow tube with a light and view lens) is placed into the back of the mouth to see the back of the throat in more detail. The examination has different names depending on the area of the body that is examined, such as laryngoscopy (larynx), pharyngoscopy (pharynx), or a nasopharyngoscopy (nasopharynx). To make the patient more comfortable, these examinations are performed using an anaesthetic spray to numb the area. If tissue looks suspicious, the doctor will take a biopsy. Tests are often done in the doctor's office; however, sometimes, an endoscopy must be performed in an operating room at a hospital using a general anaesthesia.

- Biopsy - A biopsy is the removal of a small amount of tissue for examination under a microscope. Other tests can suggest that cancer is present, but only a biopsy can make a definite diagnosis. The sample removed during the biopsy is analysed by a pathologist (a doctor who specializes in interpreting laboratory tests and evaluating cells, tissues, and organs to diagnose disease). The type of biopsy performed will depend on the location of the cancer. In a fine needle aspiration biopsy, cells are withdrawn using a thin needle inserted directly into the tumour. The cells are examined under a microscope for cancer cells (called cytologic examination).

- Oral brush biopsy - During routine dental examinations, some dentists are using a newer, simple technique to detect oral cancer in which a dentist uses a small brush to gather cell samples of a suspicious area. The specimen is then sent to a laboratory for analysis. This oral brush biopsy procedure is easy and can be done right in the dentist's chair with very little or no pain. If cancer is found using this method, it is recommended that a traditional biopsy (see above) be done to confirm the results.

- X-ray - An x-ray is a way to create a picture of the structures inside of the body, using a small amount of radiation. A dentist may take extensive x-rays of the mouth, including a panorex (panoramic view; see below).

- Barium swallow - There are two types of these tests that are generally used to look at the oropharynx and check a patient's swallowing. The first is a traditional barium swallow. During an x-ray exam, the patient is asked to swallow liquid barium so the doctor can look for any changes in the structure of the oral cavity and throat and see whether the liquid passes easily to the stomach. A modified barium swallow, or videofluoroscopy, is used to evaluate swallowing. The patient is asked to swallow liquid barium, pudding, and a cracker coated with barium.

- Panorex - This is a rotating, or panoramic, x-ray of the upper and lower jawbones to detect bone destruction from cancer or to evaluate teeth before radiation therapy or chemotherapy.

- Computed tomography (CT or CAT) scan - A CT scan creates a three-dimensional picture of the inside of the body with an x-ray machine. A computer then combines these images into a detailed, cross-sectional view that shows any abnormalities or tumours. A CT scan can also be used to measure the tumour's size. Sometimes, a contrast medium (a special dye) is injected into a patient's vein or given orally (by mouth) to provide better detail. A CT scan can help a doctor decide whether the tumour can be surgically removed and determine whether the cancer has spread to lymph nodes in the neck or lower jawbone.

- Magnetic resonance imaging (MRI) - An MRI uses magnetic fields, not x-rays, to produce detailed images of the body, especially images of soft tissue, such as the tonsils and base of the tongue. A contrast medium may be injected into a patient's vein or given orally to create a clearer picture.

- Ultrasound - An ultrasound uses sound waves to create a picture of the internal organs. This test can detect the spread of cancer to the lymph nodes in the neck (called the cervical lymph nodes).

- Positron emission tomography (PET) scan - A PET scan is a way to create pictures of organs and tissues inside the body. A small amount of a radioactive substance is injected into a patient's body. This substance is absorbed mainly by organs and tissues that use the most energy. Because cancer tends to use energy actively, it absorbs more of the radioactive substance. A scanner then detects this substance to produce images of the inside of the body.

- Panendoscopy - Is a diagnostic test used to examine the upper digestive system, including the oesophagus, stomach and first part of the small intestine. In this exam, an individual is given general anaesthesia in an operating room so that the entire region of the body can be closely inspected for cancer. Endoscopes are used to look at the throat, larynx, oesophagus and possibly the windpipe (trachea) and bronchi.

  Other parts of the nose, mouth and throat, including the trachea (windpipe) and oesophagus, are also examined during this procedure. The doctor performing the procedure will look for any visible signs of a tumour. Doctors may use a special instrument through the scope to biopsy pieces of tissue that look potentially cancerous.

(Cancer.Net; Cancer Treatment Centers of America).

Staging of Pharyngeal Cancer

A staging system is a standard way for doctors to describe and summarize how far a patient's cancer has spread. The most common system used to describe the extent of oral cavity and oropharyngeal cancers is the TNM system of the American Joint Committee on Cancer (AJCC). The TNM system for staging describes 3 key pieces of information:

- **T** indicates the size of the main (primary) **tumour** and which, if any, tissues of the oral cavity or oropharynx it has spread to.
- **N** describes the extent of spread to nearby (regional) lymph **nodes**. Lymph nodes are small bean-shaped collections of immune system cells to which cancers often spread first.
- **M** indicates whether the cancer has spread (**metastasised**) to other organs of the body. (The most common site of spread is to the lungs. The next most common sites are the liver and bones.)

Numbers or letters appear after **T**, **N**, and **M** to provide details about each of these factors:

- The numbers 0 through 4 indicate increasing severity.
- The letter X means "cannot be assessed" because the information is not available.

T categories for cancers of the lip, oral cavity, and oropharynx

TX: Primary tumour cannot be assessed; information not known

T0: No evidence of primary tumour

Tis: Carcinoma in situ. This means the cancer is still within the epithelium (the top layer of cells lining the oral cavity and oropharynx) and has not yet grown into deeper layers.

T1: Tumour is 2 cm (about ¾ inch) across or smaller

T2: Tumour is larger than 2 cm across, but smaller than 4 cm (about 1 ½ inch)

T3: Tumour is larger than 4 cm across

T4a: Tumour is growing into nearby structures. This is known as *moderately advanced local disease*.

- For oral cavity cancers: the tumour is growing into nearby structures, such as the bones of the jaw or face, deep muscle of the tongue, skin of the face, or the maxillary sinus.
- For lip cancers: the tumour is growing into nearby bone, the inferior alveolar nerve (the nerve to the jawbone), the floor of the mouth, or the skin of the chin or nose.
- For oropharyngeal cancers: the tumour is growing into the larynx (voice box), the tongue muscle, or bones such as the medial pterygoid, the hard palate, or the jaw.

T4b: The tumour has grown through nearby structures and into deeper areas or tissues. This is known as *very advanced local disease*. Any of the following may be true:

- The tumour is growing into other bones, such as the pterygoid plates and/or the skull base (for any oral cavity or oropharyngeal cancer).
- The tumour surrounds the internal carotid artery (for any oral cavity or oropharyngeal cancer).
- For lip and oral cavity cancers: the tumour is growing into an area called the *masticator space*.
- For oropharyngeal cancers: the tumour is growing into a muscle called the *lateral pterygoid muscle*.

- For oropharyngeal cancers: the tumour is growing into the nasopharynx (the area of the throat that is behind the nose).

N categories

NX: Nearby lymph nodes cannot be assessed; information not known

N0: The cancer has not spread to nearby lymph nodes

N1: The cancer has spread to one lymph node on the same side of the head or neck as the primary tumour; this lymph node is no more than 3 cm (about 1¼ inch) across

N2 includes 3 subgroups:

N2a: The cancer has spread to one lymph node on the same side as the primary tumour; the lymph node is larger than 3 cm across but no larger than 6 cm (about 2 ½ inches)

N2b: The cancer has spread to 2 or more lymph nodes on the same side as the primary tumour, but none are larger than 6 cm across

N2c: The cancer has spread to one or more lymph nodes on both sides of the neck or on the side opposite the primary tumour, but none are larger than 6 cm across

N3: The cancer has spread to a lymph node that is larger than 6 cm across

M categories

M0: No distant spread

M1: The cancer has spread to distant sites outside the head and neck region (for example, the lungs)

(National Cancer Institute; American Cancer Society).

Stage Grouping

Once the T, N, and M categories have been assigned, this information is combined by a process called stage grouping to assign an overall stage of 0, I, II, III, or IV. Stage IV is further divided into A, B, and C.

Stage 0

Tis, N0, M0: Carcinoma in situ. The cancer is only growing in the epithelium, the outer layer of oral or oropharyngeal tissue (Tis). It has not yet grown into a deeper layer or spread to nearby structures, lymph nodes (N0), or distant sites (M0).

Stage I

T1, N0, M0: The tumour is 2 cm (about ¾ inch) across or smaller (T1) and has not spread to nearby structures, lymph nodes (N0), or distant sites (M0).

Stage II

T2, N0, M0: The tumour is larger than 2 cm across but smaller than 4 cm (T2) and has not spread to nearby structures, lymph nodes (N0), or distant sites (M0).

Stage III

One of the following applies:

T3, N0, M0: The tumour is larger than 4 cm across (T3), but it hasn't grown into nearby structures or spread to the lymph nodes (N0) or distant sites (M0).

OR

T1 to T3, N1, M0:

The tumour is any size and hasn't grown into nearby structures (T1 to T3). It has spread to one lymph node on the same side of the head or neck, which is no larger than 3 cm across (N1). The cancer hasn't spread to distant sites (M0).

Stage IVA

One of the following applies:

T4a, N0 or N1, M0:

The tumour is growing into nearby structures (T4a). It can be any size. It has either not spread to the lymph nodes (N0) or has spread to one lymph node on the same side of the head or neck, which is no larger than 3 cm across (N1). The cancer hasn't spread to distant sites (M0).

OR

T1 to T4a, N2, M0:

The tumour is any size and may or may not grow into nearby structures (T1 to T4a). It has not spread to distant sites (M0). It has spread to one of the following:

- One lymph node one the same side of the head and neck that is between 3 and 6 cm across (N2a)
- One lymph node on the opposite side of the head and neck that is no more than 6 cm across (N2b)
- 2 or more lymph nodes, all of which are no more than 6 cm across. The lymph nodes can be on any side of the neck (N2c)

Stage IVB

One of the following applies:

T4b, any N, M0:

The tumour is growing into deeper areas and/or tissues (very advanced local disease - T4b). It may (or may not) have spread to lymph nodes (any N). It has not spread to distant sites (M0).

OR

Any T, N3, M0:

The tumour is any size and it may or may not have grown into other structures (any T). It has spread to one or more lymph nodes larger than 6 cm across (N3), but it hasn't spread to distant sites (M0).

Stage IVC

Any T, Any N, M1:

The tumour is any size, and it may or may not have spread to lymph nodes. It has spread to distant sites, most commonly the lungs.

(National Cancer Institute; American Cancer Society).

Recurrent (relapsed) Cancer

This is not an actual stage in the **TNM** system. Recurrent (relapsed) disease means that the cancer has come back (recurred) after treatment. Recurrent oral cavity or oropharyngeal

cancer may return in the mouth or throat (local recurrence), in nearby lymph nodes (regional recurrence) or in another part of the body, such as the lungs (distant recurrence).
(American Cancer Society).

Treatment of Pharyngeal Cancer
Treatment is based on many factors, such as the location and stage of the cancer, the type of cells involved, overall health, and personal preferences. Benefits and risks of each of the options should be discussed with the treating doctor.

Radiation therapy - Radiation therapy uses high-energy beams, such as X-rays, to deliver radiation to the cancer cells, causing them to die. Radiation therapy can come from a large machine outside your body (external beam radiation). Or radiation therapy can come from small radioactive seeds and wires that can be placed inside the body, near the cancer (brachytherapy).

For early-stage pharyngeal (throat) cancers, radiation therapy may be the only treatment necessary. For more advanced throat cancers, radiation therapy may be combined with chemotherapy or surgery. In very advanced throat cancers, radiation therapy may be used to reduce signs and symptoms and make the patient more comfortable.

Surgery - The types of surgical procedures that may be considered depend on the location and stage of the cancer. Options may include:

- Surgery for early-stage throat cancer. Throat cancer that is confined to the surface of the throat or the vocal cords may be treated surgically using endoscopy. The doctor may insert a hollow endoscope into the throat or voice box and then pass special surgical tools or a laser through the scope. Using these tools, the doctor can scrape off, cut out or, in the case of the laser, vaporise very superficial cancers.

- Surgery to remove all or part of the voice box (laryngectomy) - For smaller tumours, the doctor may remove the part of the voice box that is affected by cancer, leaving as much of the voice box as possible. The doctor may be able to preserve the patient's ability to speak and breathe normally. For larger, more-extensive tumours, it may be necessary to remove the entire voice box. The windpipe is then attached to a hole (stoma) in the throat to allow the person to breathe (tracheotomy). If the entire larynx is removed, the patient will have several options for restoring speech. He/she can work with a speech pathologist to learn to speak without a voice box.

  Please refer to the CANSA **Fact Sheet on Cancer of the Larynx.**

- Surgery to remove all or part of the throat (pharyngectomy) - Smaller throat cancers may require removing only part of your throat during surgery. Parts that are removed may be reconstructed in order to allow you to swallow food normally. Surgery to remove your entire throat usually includes removal of your voice box as well. Your doctor may be able to reconstruct your throat to allow you to swallow food.

- Surgery to remove cancerous lymph nodes (neck dissection) - If throat cancer has spread deep within the neck, the doctor may recommend surgery to remove some or all of the lymph nodes to see if they contain cancer cells. Surgery carries a risk of

bleeding and infection. Other possible complications, such as difficulty speaking or swallowing, will depend on the specific procedure the patient has to undergo.

Reconstructive surgery can help restore appearance and rehabilitate speech and swallowing function. Prosthetic devices in the mouth may replace removed portions of teeth, gums and jaw. In more advanced cases, a patient may need to use tubes for feeding and breathing and an artificial voice aid for speaking.

Chemotherapy - Chemotherapy uses chemicals to kill cancer cells. Chemotherapy is often used along with radiation therapy in treating throat cancers. Certain chemotherapy drugs make cancer cells more sensitive to radiation therapy. But combining chemotherapy and radiation therapy increases the side effects of both treatments. Discuss with your doctor the side effects you're likely to experience and whether combined treatments will offer benefits that outweigh those effects.

Targeted drug therapy - Targeted drugs treat throat cancer by taking advantage of specific defects in cancer cells that fuel the cells' growth. Cetuximab (Erbitux) is one targeted therapy approved for treating throat cancer in certain situations. Cetuximab stops the action of a protein that's found in many types of healthy cells, but is more prevalent in certain types of throat cancer cells.

Other targeted drugs are being studied in clinical trials. Targeted drugs can be used in combination with chemotherapy or radiation therapy.
(Mayo Clinic; University of California San Francisco).

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.

Types of Clinical Trials
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

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