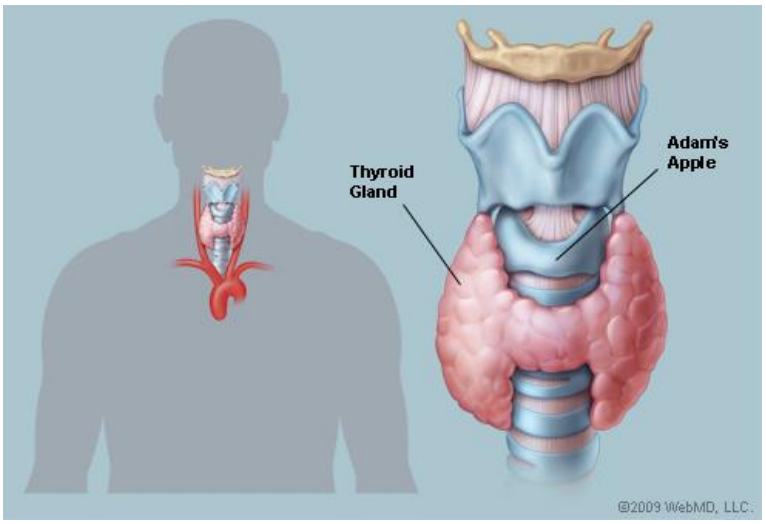
Cancer Association of South Africa (CANSA)

Research • Educate • Support

Fact Sheet
on
Cancer of the Thyroid

Introduction

The thyroid is a butterfly-shaped gland that sits low on the front of the neck. The thyroid lies below the Adam's apple, along the front of the windpipe. It has two side lobes, connected by a bridge (isthmus) in the middle. When the thyroid is its normal size, it cannot be felt.



[Picture Credit: Thyroid Gland]

Brownish-red in colour, the thyroid is rich with blood vessels. Nerves important for voice quality also pass through the thyroid.

The thyroid secretes several hormones, collectively called thyroid hormones. The main hormone is thyroxine, also called T4. Thyroid hormones act throughout the body, influencing metabolism, growth and development, and body temperature. During infancy and childhood, adequate thyroid hormone is crucial for brain development.

The C cells in the thyroid make calcitonin. This hormone plays a small role in keeping a healthy level of calcium in the body. Four or more tiny parathyroid glands are on the back of the thyroid. These glands make parathyroid hormone. This hormone plays a big role in helping the body maintain a healthy level of calcium.

Thyroid Cancer

Thyroid cancer is when cancer develops in the cells of the thyroid. Cancer begins in cells, the building blocks that make up tissues. Tissues make up the thyroid and other organs of the body. Normal

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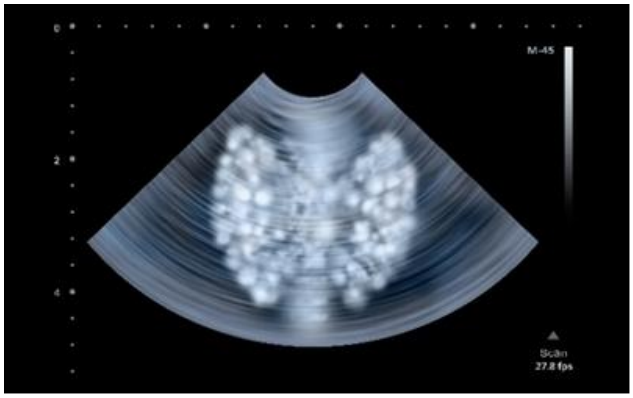
thyroid cells grow and divide to form new cells as the body needs them. When normal cells grow old or get damaged, they die, and new cells take their place.

Sometimes, this process goes wrong. New cells form when the body does not need them, and old or damaged cells do not die as they should. The build-up of extra cells often forms a mass of tissue called a nodule. It may also be called a growth or tumour. Most thyroid nodules are benign. Benign nodules are not cancer (malignant).



[Picture Credit: Thyroid]

Thyroid cancer cells can spread by breaking away from the thyroid tumour. They can travel through lymph vessels to nearby lymph nodes. They can also spread through blood vessels to the lungs, liver, or bones. After spreading, cancer cells may attach to other tissues and grow to form new tumours that may damage those tissues.

Tsang, V.H.M., Gild, M., Glover, A., Clifton-Bligh, R. & Robinson, B.G. 2020.
"COVID-19 has modified the way we practice medicine. For thyroid cancer, there have been several significant impacts. First, the diagnosis has been delayed due to social isolation, reduced access to investigations and staff redeployment. Secondly, treatment planning has needed to take into account the risk to patients and/or staff of nosocomial transmission of the virus. Finally, there are some specific concerns with respect to interactions between the virus, its treatments and cancer. This mini-review aims to address each of these impacts and to provide some guidance and confidence to our patients and colleagues during this challenging time."

Araque, K.A., Gubbi, S. & KlubooGwiezdzinska, J. 2020.
"The diagnostic modalities, stratification tools, and treatment options for patients with thyroid cancer have rapidly evolved since the development of the American Thyroid Association (ATA) guidelines in 2015. This review compiles newer concepts in diagnosis, stratification tools and treatment options for patients with differentiated thyroid cancer (DTC), medullary thyroid carcinoma (MTC) and anaplastic thyroid cancer (ATC). Newer developments apply precision medicine in thyroid cancer patients to avoid over-treatment in low risk disease and under-treatment in high risk disease. Among novel patient-tailored therapies are selective RET inhibitors that have shown efficacy in the treatment of MTC with limited systemic toxicity compared with non-specific tyrosine kinase inhibitors. The combination of BRAF and MEK inhibitors have revolutionized management of *BRAF V600E* mutant ATC. Several immunotherapeutic agents are being actively investigated in the treatment of all forms of thyroid cancer."

Botezatu, A., Iancu, I.V., Plesa, A., Manda, D., Popa, O., Bostan, M., Mihaila, M., Albulescu, A., Fudulu, A., Vladoiu, S.V., Huica, I., Dobrescu, R., Anton, G. & Badiu, C. 2019.
BACKGROUND: Thyroid carcinoma is the most common endocrine malignancy worldwide. Changes in DNA methylation can cause silencing of normally active genes, especially tumour suppressor genes (TSG) or activation of normally silent genes.
OBJECTIVE: The aim of this study is to evaluate the degree of promoter methylation for a panel of markers for thyroid neoplasms and to establish their relationship with thyroid oncogenesis.

METHODS: To generate a comprehensive DNA methylation signature of TSGs involved in thyroid neoplasia, we use Human TSG EpiTect Methyl II Signature PCR Array-Qiagen for 24 samples (follicular adenomas and papillary thyroidcarcinomas) compared with normal thyroid tissue. We extended the evaluation for three TSGs (TP73, WIF1, PDLIM4) using qMS-PCR. Statistical analysis was performed with GraphPad Prism.
RESULTS: We noted four important genes NEUROG1, ESR1, RUNX3, MLH1, which presented methylated promoter in tumour samples compared to normal. We found new characteristic of thyroid tumours: methylation of TP73, WIF1 and PDLIM4 TSGs, which can contribute to thyroid neoplasia. A significant correlation between BRAF V600E mutation and RET/PTC rearrangements with TIMP3 and CDH13, RARB methylation, respectively was observed.
CONCLUSIONS: TSGs promoter hypermethylation is a hallmark of cancer and a test that uses methylation quantification method is suitable for diagnosis and prognosis of thyroid cancer.

Tumour Grade and Tumour Stage
Tumour grade and stage are terms used to describe the severity of a tumour, while tumour grade describes the appearance of cancerous cells in the tissue by examining them under a microscope.

Tumour stage encompasses:

- The location of the tumour.
- The size and/or extent of the original tumour.
- Whether cancer cells have spread to lymph nodes or anywhere else in the body.
- The number of tumours present.

Doctors use tumour grade, cancer stage, and a patient's age and general health to decide the course of treatment for the patient and determine prognosis. Prognosis describes all factors including the disease course, cure rate, chances of survival, and risk of recurrence of cancer.

What are the cancer stages?
Different systems of cancer staging are used to describe the types of cancer. Below is a common method in which stages are ranged from 0 to IV.

- Stage 0: The tumour is confined to its place of origin (in situ) and has not spread to nearby tissue.
- Stage I: The tumour is located only in the original organ, is small, and has not spread.
- Stage II: The size of the tumour is large but has not spread.
- Stage III: The tumour has become larger and may have spread to surrounding tissues and/or lymph nodes.
- Stage IV: The tumour has spread to other distant organs of the body, which is known as the metastasis stage.

TNM staging
Another common staging method used for cancer is the TNM system, which stands for tumour, node (which means spread of the tumour to lymph nodes), and metastasis. When a patient's cancer is staged using the TNM system, a number will be present along with the letter. This number signifies the extent of the disease in each category - tumour, node, and metastases.

Another system of cancer staging divides cancer into five stages, which include:

- In situ: Abnormal cells are present but have not spread to nearby tissue.
- Localized: Cancer is located only in the original organ and shows no sign of its spread.
- Regional: Cancer has spread to nearby lymph nodes, tissues, or organs.
- Distant: Cancer has spread to distant parts of the body.
- Unknown: The stage cannot be figured out due to a lack of enough information.

What are the cancer grades?

Cancer grades are based on examination of the suspected tissue sample under a microscope. This involves surgically removing a piece of the suspected cancerous tissue and sending it to the lab for analysis. The entire procedure is known as a biopsy.

A doctor who specializes in diagnostic tests (pathologist) examines the cells of the tissue and determines whether they are harmless (benign or noncancerous) or harmful (malignant or cancerous). They describe the microscopic appearance of the cells and assign a numerical "grade" to most cancers.

Generally, a lower grade indicates slow-growing cancer and a higher grade indicates fast-growing cancer.

The most commonly used grading system is as follows:

- Grade I: Cancer cells that look like normal cells but are not growing rapidly.
- Grade II: Cancer cells that don't look like normal cells with their growth being faster than normal cells.
- Grade III: Cancer cells that look abnormal and have the potential to grow rapidly or spread more aggressively.

Sometimes, the following system can be used:

- GX: Grade cannot be assessed (undetermined grade)
- G1: Well-differentiated (low grade)
- G2: Moderately differentiated (intermediate grade)
- G3: Poorly differentiated (high grade)
- G4: Undifferentiated (high grade)

Incidence of Thyroid Cancer in South Africa

According to the outdated National Cancer Registry (2017), known for under reporting, the following number of cases of the thyroid gland was histologically diagnosed in South Africa during 2017. Histologically diagnosed means that a tissue sample (biopsy) was forwarded to an approved pathology laboratory where a specially trained pathologist confirmed a cancer diagnosis:

Group - Males 2017	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All males	188	1:1 035	0,47%
Asian males	13	1:783	1,34%
Black males	48	1:2 555	0,35%
Coloured males	24	1:940	0,51%
White males	103	1:302	0,49%

Group - Females 2017	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All females	559	1:506	1,34%
Asian females	41	1:225	3,18%
Black females	205	1:1 035	1,05%
Coloured females	73	1:387	1,56%
White females	240	1:136	1,41%

The frequency of histologically diagnosed cases of cancer of the thyroid gland in South Africa for 2017 was as follows (National Cancer Registry, 2017):

Group - Males 2017	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	7	4	6	18	30	43	24	7
Asian males	0	3	1	4	3	1	1	0
Black males	2	2	10	7	14	8	4	1
Coloured males	1	1	4	5	3	6	6	2
White males	2	7	11	16	21	27	18	1

Group - Females 2017	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	9	54	114	118	113	77	58	16
Asian females	1	6	13	10	6	3	2	0
Black females	4	18	37	50	40	26	21	9
Coloured females	1	7	18	13	12	11	8	3
White females	3	23	46	45	55	37	27	4

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.

According to **Bruni, *et al*.,** (2019), the burden of cancer of the Thyroid for South Africa for 2018 is estimated as (based on Globocan estimates):

- Annual number of cancer of the Thyroid cases 2 408
- Annual number of cancer of the Thyroid deaths 157

Deng, Y., Li, H., Wang, M., Li, N., Tian, T., Wu, Y., Xu, P., Yang, S., Zhai, Z., Zhou, L., Hao, Q., Song, D., Jin, T., Lyu, J. & Dai, Z. 2020.

Importance: Thyroid cancer is the most pervasive endocrine cancer worldwide. Studies examining the association between thyroid cancer and country, sex, age, sociodemographic index (SDI), and other factors are lacking.

Objective: To examine the thyroid cancer burden and variation trends at the global, regional, and national levels using data on sex, age, and SDI.

Design, setting, and participants: In this cross-sectional study, epidemiologic data were gathered using the Global Health Data Exchange query tool, covering persons of all ages with thyroid cancer in 195 countries and 21 regions from January 1, 1990, to December 31, 2017; data analysis was completed on October 1, 2019. All participants met the Global Burden of Disease Study inclusion criteria.

Main outcomes and measures: Outcomes included incidence, deaths, and disability-adjusted life-years (DALYs) of thyroid cancer. Measures were stratified by sex, region, country, age, and SDI. The

estimated annual percentage changes (EAPCs) and age-standardized rates were calculated to evaluate the temporal trends.

Results: Increases of thyroid cancer were noted in incident cases (169%), deaths (87%), and DALYs (75%). Age-standardized incidence rate (ASIR) showed an upward trend over time, with an EAPC of 1.59 (95% CI, 1.51-1.67); decreases were noted in EAPCs of age-standardized death rate (-0.15; 95% CI, -0.19 to -0.12) and age-standardized DALY rate (-0.11; 95% CI, -0.15 to -0.08). Almost half (41.73% for incidence, 50.92% for deaths, and 54.39% for DALYs) of the thyroid cancer burden was noted in Southern and Eastern Asia. In addition, females accounted for most of the thyroid cancer burden (70.22% for incidence, 58.39% for deaths, and 58.68% for DALYs) and increased by years in this population, although the ASIR of males with thyroid cancer (EAPC, 2.18; 95% CI, 2.07-2.28) increased faster than that of females (EAPC, 1.38; 95% CI, 1.30-1.46). A third (34%) of patients with thyroid cancer resided in countries with a high SDI, and most patients were aged 50 to 69 years, which was older than the age in other quintiles (high SDI quintile compared with all other quintiles, P<.05). The most common age at onset of thyroid cancer worldwide was 15 to 49 years in female individuals compared with 50 to 69 years in male individuals (P<.05). Death from thyroid cancer was concentrated in participants aged 70 years or older and increased by years (average annual percentage change, 0.10; 95% CI, 0.01-0.21; P<.05). Furthermore, people in lower SDI quintiles developed thyroid cancer and died from it earlier than those in other quintiles (high and high-middle SDI vs low and low-middle SDI, P<.05).

Conclusions and relevance: Data from this study suggest considerable heterogeneity in the epidemiologic patterns of thyroid cancer across sex, age, SDI, region, and country, providing information for governments that may help improve national and local cancer control policies.

Signs and Symptoms of Thyroid Cancer

Thyroid cancer does not always have symptoms, so it can be hard to detect and diagnose. In fact, some of the possible symptoms are not actually caused by thyroid cancer itself. Instead, these symptoms can be caused by a thyroid nodule - and thyroid nodules are not necessarily cancerous.

People may visit a doctor because they notice one or more of the following symptoms and signs:

Lump in the Neck - Not all thyroid nodules are big enough to cause a noticeable lump. The most common way that a thyroid lump (and potential thyroid cancer) is detected, however, is when a doctor performs a thyroid examination and feels the thyroid.

Swollen Lymph Node - Swollen lymph nodes in the neck are another symptom of thyroid cancer (a symptom not related to thyroid nodules). Thyroid cancer can spread to the lymph nodes. The lymph nodes in one's neck become swollen when one has a cold or sore throat, for example. When the infection is gone, they should return to their normal size, so if the lymph nodes in one's neck stay enlarged for an extended period one should talk to one's doctor.

[Picture Credit: Lump in Neck]

Hoarse Voice - The thyroid gland sits just below the larynx (more commonly known as the voice box or Adam's apple). A thyroid nodule (which may be thyroid cancer) may be pressing on the voice box, causing hoarseness or voice changes. This is an uncommon way that thyroid cancer is detected.

Difficulty Swallowing or Breathing - The thyroid is on top of the trachea or windpipe. A developing thyroid cancer may put pressure on the trachea, making breathing more difficult. The oesophagus is below the trachea, so again, a developing thyroid cancer can cause trouble swallowing. This is also an uncommon way that thyroid cancer is detected.

Risk Factors for Thyroid Cancer
The following risk factors for thyroid cancer have been identified:

Gender and age - for unclear reasons thyroid cancers (like almost all diseases of the thyroid) occur about 3 times more often in women than in men. Thyroid cancer can occur at any age, but the risk peaks earlier for women (who are most often in their 40s or 50s when diagnosed) than for men (who are usually in their 60s or 70s).

Johar, J., Britton, H. & Wiseman, S.M. 2020.
"Differentiated thyroid cancer (DTC) has long been recognized as having a worse prognosis in older people. We retrospectively evaluated the clinical and pathological characteristics of 973 sequentially treated patients with primary DTC stratified into 2 age groups, ≥ 55 or < 55 years, based on the current American Joint Committee on Cancer (AJCC) DTC staging system. We found that older patients had a higher frequency of extrathyroidal cancer extension and larger cancers, and that their cancers were less commonly completely resectable."

Diet low in iodine - follicular thyroid cancers are more common in areas of the world where people's diets are low in iodine. A diet low in iodine may also increase the risk of papillary cancer if the person also is exposed to radioactivity.

Radiation - exposure to radiation is a proven risk factor for thyroid cancer. Sources of such radiation include certain medical treatments and radiation fallout from power plant accidents or nuclear weapons.

Hereditary conditions and family history - several inherited conditions have been linked to different types of thyroid cancer, as has family history. Still, most people who develop thyroid cancer do not have an inherited condition or a family history of the disease.

Medullary thyroid cancer
About 1 out of 3 medullary thyroid carcinomas (MTCs) result from inheriting an abnormal gene.

Other thyroid cancers
People with certain inherited medical conditions have a higher risk of more common forms of thyroid cancer.

Higher rates of thyroid cancer occur among people with uncommon genetic conditions such as:

- familial adenomatous polyposis (FAP): People with this syndrome develop many colon polyps and have a very high risk of colon cancer. They also have an increased risk of some other cancers, including papillary thyroid cancer. *Gardner syndrome* is a subtype of FAP in which patients also get certain benign tumours. Both Gardner syndrome and FAP are caused by defects in the gene *APC*.

- Cowden disease: People with this syndrome have an increased risk of thyroid, endometrial (uterine), and breast cancers. The thyroid cancers tend to be either the papillary or follicular type. This syndrome is caused by defects in the gene *PTEN*.

Papillary and follicular thyroid cancers do seem to run in some families. Having a first-degree relative (parent, brother, sister, or child) with thyroid cancer, even without a known inherited syndrome in the family, increases one's risk for thyroid cancer. The genetic basis for these cancers is not totally clear.

Diagnosis of Thyroid Cancer

Diagnosis of thyroid cancer typically involves a number of procedures and tests.

Physical Exam - the doctor should conduct a thorough physical examination, including palpation of the thyroid to feel for enlargement and lumps, as well as the gland's size and firmness. The doctor will also look for any enlarged lymph nodes in the neck.

Biopsy - doctors often will do a biopsy of suspicious thyroid nodules, to evaluate for potential cancer. Typically thyroid nodules are biopsied using a needle, in a procedure known as 'fine needle aspiration biopsy' -- sometimes abbreviated FNA. Some patients have a surgical biopsy, where the nodule, or the thyroid gland itself, is removed surgically.

Erkinuresin, T. & Demirci, H. 2020.

"Background Routine application of fine needle aspiration cytology (FNAC) has decreased unnecessary referral of thyroid nodules for surgical treatment and has also increased the cancer rates found in surgery materials. Success of thyroid FNAC depends on skilled aspiration, skilled cytological interpretation and rational analysis of cytological and clinical data. The aim of this study was to determine the diagnostic accuracy rates of thyroid FNAC results obtained in our institution. Methods The data from FNAC and thyroidectomy reports of patients presenting with goiter and who had been evaluated from 1st January 2014 to 1st March 2018 were used. There were 149 patients in total who had undergone thyroidectomy following FNAC. The Bethesda System for Reporting Thyroid Cytology was used in all cytological diagnoses. Results The sensitivity of thyroid FNAC for malignant cases was 57.89%, specificity was 88.10%, false-positive rate was 11.90%, false-negative rate was 42.11%, positive predictive value was 52.38%, negative predictive value was 90.24% and accuracy rate was 82.52%. "Focus number" variable was detected as the factor that affected the accurate prediction of FNAC and thyroidectomy results by the pathologist. Conclusions This study showed that there was a moderate conformity between thyroid FNAC and thyroidectomy cyto-histopathological diagnosis in malignant cases. As two or more nodules have a negative effect on the physician's diagnosis of malignant nodules, we think that a more sensitive

approach is needed in the determination of these cases. Sampling defects may affect this non-matching."

Imaging Tests - A variety of imaging scans are used to evaluate thyroid nodules for possible thyroid cancer. These may include:

- Nuclear scan, also known as radioactive iodine uptake (RAI-U) scan. Nodules that absorb more radioactive iodine, and therefore are more visible, are known as "hot nodules" and are more likely to be benign.
- CT scan, known as computed tomography or a "cat scan," is a specialized type of x-ray that is sometimes used to evaluate the thyroid. A CT scan can't detect smaller nodules, but may help detect and diagnose a goiter, or larger thyroid nodules.
- Magnetic resonance imaging (MRI), can help detect enlargement in the thyroid, as well as tumours, tumour size, and may be able to detect tumour spread.
- Thyroid ultrasound, can tell whether a nodule is a fluid-filled cyst, or a mass of solid tissue, but it cannot determine if a nodule or lump is malignant.

Wang, L., Kou, H., Chen, W., Lu, M. Zhou, L. & Zou, C. 2020.
PURPOSE: To explore the clinical value of ultrasound in the diagnosis of medullary thyroid carcinoma by comparing with enhanced computed tomography.
METHODS: This retrospective study was performed on 62 patients with pathologically confirmed medullary thyroid carcinoma. All patients underwent ultrasound and enhanced computed tomography examinations before surgery. The findings of the pathologic examination of resected specimens were considered as gold standard and were compared with the results of these 2 methods.
RESULTS: There were 73 medullary thyroid carcinoma lesions and 29 benign lesions in 62 patients. In all, 55 of 73 medullary thyroid carcinoma lesions and 27 of 29 benign lesions were correctly diagnosed by ultrasound; and 45 of 73 medullary thyroid carcinoma lesions and 24 of 29 benign lesions were correctly diagnosed by enhanced computed tomography. The accuracy of ultrasound and enhanced computed tomography was 80.4% and 67.6%, respectively. There was significant difference between 2 methods ($P < .05$).
CONCLUSIONS: Ultrasound can be used to observe the location, number, size, shape, border, internal echo, calcification, and blood flow of the lesion. It is a convenient, inexpensive, and nonradiative method with higher accuracy than enhanced computed tomography.

Blood Tests - blood tests cannot diagnose thyroid cancer itself, or detect a cancerous thyroid nodule. Thyroid stimulating hormone (TSH) blood tests, however, may be used to evaluate the thyroid's activity and test for hypothyroidism or hyperthyroidism.

Other Tests - when medullary thyroid cancer is suspected, doctors will typically test for high levels of calcium, as this can be an indicator. They may also do genetic testing to identify the abnormal gene associated with some cases of medullary thyroid cancer.

How Thyroid Cancer Can Spread
Should Cancer of the thyroid spread to organs in the body, it may spread as indicated below:

Cancer Type:	Main Sites of Metastasis (Spread)
Bladder	Bone, liver, lung
Breast	Bone, brain, liver, lung
Colon	Liver, lung
Colorectal	Liver, lung, peritoneum (lining of abdomen)
Kidney	Adrenal gland, bone, brain, liver, lung
Lung	Adrenal gland, bone, brain, liver, other lung
Melanoma	Bone, brain, liver, lung, skin, muscle
Ovary	Liver, lung, peritoneum (lining of abdomen)
Pancreas	Liver lung, peritoneum (lining of abdomen)
Prostate	Adrenal gland, bone, liver, lung
Stomach	Liver, lung, peritoneum (lining of abdomen), ovaries
Thyroid	Bone, liver, lung
Uterus	Boner, liver, lung, peritoneum (lining of abdomen), vagina
Non-melanoma skin cancer	Very rare: lymph nodes, lung, bone (if in head/neck region)

Treatment of Thyroid Cancer

Thyroid cancer treatment options depend on the type and stage of the thyroid cancer, the overall health of the patient and his/her preferences. Most cases of thyroid cancer can be cured with treatment. Treatment may include:

Surgery

Most people with thyroid cancer undergo surgery to remove all or most of the thyroid.

Kaliszewski, K., Wojtczak, B., Sutkowski, K., Rudnicki, J. 2020.

"The prevalence of thyroid cancer, especially in women, is increasing dramatically. Therefore, patients often undergo thyroidectomy upon diagnosis. However, the cosmetic outcome after surgery is of particular concern for many patients. Thus, minimally invasive procedures for treating thyroid disease have been established in recent decades. Total endoscopic and robotic procedures have been slowly and successively introduced while meeting all oncological criteria. Our analysis of the advantages and disadvantages of scarless surgical procedures suggests that the cosmetic aspects of these surgeries will continue to become more important. This review assesses the recent findings regarding the roles of endoscopic and robotic procedures in thyroid cancer surgery."

Thyroid hormone therapy

After thyroid cancer surgery, patients are given thyroid hormone medication for life.

Radioactive iodine

Radioactive iodine treatment uses large doses of a form of iodine that is radioactive. Radioactive iodine treatment is often used after thyroidectomy to destroy any remaining healthy thyroid tissue, as well as microscopic areas of thyroid cancer that were not removed during surgery. Radioactive iodine treatment may also be used to treat thyroid cancer that recurs after treatment or that spreads to other areas of the body.

External radiation therapy

Radiation therapy can also be given externally using a machine that aims high-energy beams at precise points on the body. Called external beam radiation therapy, this treatment is typically administered a few minutes at a time, five days a week, for about six weeks.

Chemotherapy

Chemotherapy is a drug treatment that uses chemicals to kill cancer cells. Chemotherapy is typically given as an infusion through a vein. Chemotherapy is not commonly used in the treatment of thyroid cancer, but it may benefit some people who do not respond to other, more standard therapies.

Bautista, L., Knippler, C.M. & Ringel, M.D. 2020.

"The family of p21-activated kinases (PAKs) are oncogenic proteins that regulate critical cellular functions. PAKs play central signaling roles in the integrin/CDC42/Rho, ERK/MAPK, PI3K/AKT, NF-κB, and Wnt/β-catenin pathways, functioning both as kinases and scaffolds to regulate cell motility, mitosis and proliferation, cytoskeletal rearrangement, and other cellular activities. PAKs have been implicated in both the development and progression of a wide range of cancers, including breast cancer, pancreatic melanoma, thyroid cancer, and others. Here we will discuss the current knowledge on the structure and biological functions of both group I and group II PAKs, as well as the roles that PAKs play in oncogenesis and progression, with a focus on thyroid cancer and emerging data regarding BRAF/PAK signaling."

Targeted therapy

In general, thyroid cancers do not respond well to chemotherapy. But exciting data are emerging about some newer targeted drugs. Unlike standard chemotherapy drugs, which work by attacking rapidly growing cells (including cancer cells), these drugs attack specific targets on cancer cells.

PDQ Adult Treatment Editorial Board. 2019.

Six types of standard treatment for thyroid cancer are used:

Surgery

Surgery is the most common treatment for thyroid cancer. One of the following procedures may be used:

- Lobectomy: Removal of the lobe in which thyroid cancer is found. Lymph nodes near the cancer may also be removed and checked under a microscope for signs of cancer.
- Near-total thyroidectomy: Removal of all but a very small part of the thyroid. Lymph nodes near the cancer may also be removed and checked under a microscope for signs of cancer.
- Total thyroidectomy: Removal of the whole thyroid. Lymph nodes near the cancer may also be removed and checked under a microscope for signs of cancer.
- Tracheostomy: Surgery to create an opening (stoma) into the windpipe to help you breathe. The opening itself may also be called a tracheostomy.

Radiation therapy, including radioactive iodine therapy

Radiation therapy is a cancer treatment that uses high-energy X-rays or other types of radiation to kill cancer cells or keep them from growing. There are two types of radiation therapy:

- External radiation therapy uses a machine outside the body to send radiation toward the cancer. Sometimes the radiation is aimed directly at the tumour during surgery. This is called intraoperative radiation therapy.
- Internal radiation therapy uses a radioactive substance sealed in needles, seeds, wires, or catheters that are placed directly into or near the cancer.

Radiation therapy may be given after surgery to kill any thyroid cancer cells that were not removed. Follicular and papillary thyroid cancers are sometimes treated with radioactive iodine (RAI) therapy. RAI is taken by mouth and collects in any remaining thyroid tissue, including thyroid cancer cells that have spread to other places in the body. Since only thyroid tissue takes up iodine, the RAI destroys thyroid tissue and thyroid cancer cells without harming other tissue. Before a full treatment dose of RAI is given, a small test-dose is given to see if the tumour takes up the iodine.
The way the radiation therapy is given depends on the type and stage of the cancer being treated. External radiation therapy and radioactive iodine (RAI) therapy are used to treat thyroid cancer.

Chemotherapy

Chemotherapy is a cancer treatment that uses drugs to stop the growth of cancer cells, either by killing the cells or by stopping them from dividing. When chemotherapy is taken by mouth or injected into a vein or muscle, the drugs enter the bloodstream and can reach cancer cells throughout the body (systemic chemotherapy). When chemotherapy is placed directly into the cerebrospinal fluid, an organ, or a body cavity such as the abdomen, the drugs mainly affect cancer cells in those areas (regional chemotherapy).
The way the chemotherapy is given depends on the type and stage of the cancer being treated.

Thyroid hormone therapy

Hormone therapy is a cancer treatment that removes hormones or blocks their action and stops cancer cells from growing. Hormones are substances made by glands in the body and circulated in the bloodstream. In the treatment of thyroid cancer, drugs may be given to prevent the body from making thyroid stimulating hormone (TSH), a hormone that can increase the chance that thyroid cancer will grow or recur.
Also, because thyroid cancer treatment kills thyroid cells, the thyroid is not able to make enough thyroid hormone. Patients are given thyroid hormone replacement pills.

Targeted therapy

Targeted therapy is a type of treatment that uses drugs or other substances to identify and attack specific cancer cells without harming normal cells. There are different types of targeted therapy:

- Tyrosine kinase inhibitor. Tyrosine kinase inhibitor therapy blocks signals needed for tumours to grow. Sorafenib, lenvatinib, vandertanib, and cabozantinib are used to treat certain types of thyroid cancer. New types of tyrosine kinase inhibitors are being studied to treat advanced thyroid cancer.
- Protein kinase inhibitor**.** Protein kinase inhibitor therapy blocks proteins needed for cell growth and may kill cancer cells. dabrafenib and tramatinib are used to treat anaplastic thyroid cancer in patients with a certain mutation in the BRAF gene.

Watchful waiting

Watchful waiting is closely monitoring a patient's condition without giving any treatment until signs or symptoms appear or change.

New types of treatment are being tested in clinical trials.

Immunotherapy

Immunotherapy is a treatment that uses the patient's immune system to fight cancer. Substances made by the body or made in a laboratory are used to boost, direct, or restore the body's natural defenses against cancer. This type of cancer treatment is also called biotherapy or biologic therapy. Immunotherapy is being studied as a treatment for thyroid cancer.

About Clinical Trials

Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:

- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers
- Tests to find new ways of screening for cancer

The South African National Clinical Trials Register provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: www.sanctr.gov.za/

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.

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