

<b>Title</b>	Basics of Thyroid Cancer
<b>Authored By</b>	Anita Rothera RNC, BS, CDE
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## Purpose

The goal of this course is to help healthcare professionals learn about thyroid cancer symptoms, diagnosis, stages, treatment and more.

## Objectives

1. Identify four common symptoms of thyroid cancer.
  2. Discuss types of thyroid cancer and incidence.
  3. State the function of the thyroid gland and how it works.
  4. Describe three stages of cancer of the thyroid.
  5. State three risk factors associated with thyroid cancer.
  6. Discuss four treatment options for thyroid cancer.
  7. Identify four tests used for screening and diagnosis of thyroid cancer.
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## Thyroid Cancer

The thyroid gland is a small gland, normally weighing less than one ounce, located in the front of the neck. It is made up of two halves, called lobes, that lie along the windpipe (trachea) and are joined together by a narrow band of thyroid tissues, known as the isthmus.

The thyroid is situated just below the "Adams apple" or larynx. During development (inside the womb) the thyroid gland originates in the back of the tongue, but it normally migrates to the front of the neck before birth. Sometimes it fails to migrate properly and is located high in the neck or even in the back of the tongue (lingual thyroid). This is very rare. At other times it may migrate too far and ends up in the chest (this is also very rare).

The function of the thyroid gland is to take iodine, found in many foods, and convert it into thyroid hormones: thyroxine (T4) and triiodothyronine (T3). Thyroid cells are the only cells in the body which can absorb iodine. These cells combine iodine and the amino acid tyrosine to make T3 and T4. T3 and T4 are then released into the blood stream and are transported throughout the body where they control metabolism (conversion of oxygen and calories to energy). Every cell in the body depends upon thyroid hormones for regulation of their metabolism. The normal thyroid gland produces about 80% T4 and about 20% T3, however, T3 possesses about four times the hormone "strength" as T4.

The thyroid gland is under the control of the pituitary gland, a small gland the size of a peanut at the base of the brain. When the level of thyroid hormones drops too low, the pituitary gland produces Thyroid Stimulating Hormone (TSH) which stimulates the thyroid gland to produce more hormones. Under the influence of TSH, the thyroid will manufacture and secrete T3 and T4 thereby raising their blood levels. The pituitary senses this and responds by decreasing its TSH production. One can imagine the thyroid gland as a furnace and the pituitary gland as the

thermostat. Thyroid hormones are like heat. When the heat gets back to the thermostat, it turns the thermostat off. As the room cools (the thyroid hormone levels drop), the thermostat turns back on (TSH increases) and the furnace produces more heat (thyroid hormones).

The pituitary gland itself is regulated by another gland, known as the hypothalamus. The hypothalamus is part of the brain and produces TSH Releasing Hormone (TRH) which tells the pituitary gland to stimulate the thyroid gland (release TRH). One might imagine the hypothalamus as the person who regulates the thermostat since it tells the pituitary gland at what level the thyroid should be set.

Many cases of thyroid cancer can be found early. Most thyroid cancers are now found much earlier than in the past and can be treated successfully. Although it's unusual, some thyroid cancers may not cause symptoms until after reaching an advanced stage. Most early thyroid cancers are found when patients ask their doctors about nodules they have noticed. Others are found by healthcare professionals during a routine checkup. No blood tests are regularly recommended for early detection of sporadic (not familial) thyroid cancers. Removing the thyroid gland in children with a family history of thyroid cancer is effective in preventing a cancer that might otherwise be fatal.

### **Signs and Symptoms of Thyroid Cancer**

Prompt attention to signs and symptoms is the best approach to early diagnosis of most thyroid cancers. Thyroid cancer can cause any of the following signs or symptoms:

- A lump in the neck, sometimes growing rapidly
- A pain in the neck, sometimes going up to the ears
- Hoarseness
- Trouble swallowing
- Breathing problems (feeling as if one were "breathing through a straw")
- A cough that continues and is not due to a cold

Other cancers of the neck area and many noncancerous conditions can cause some of the same symptoms. Thyroid nodules are common, and they are almost always benign. (1)

### **Types of Thyroid Cancer**

Females are more likely to have thyroid cancer at a ratio of three to one. Thyroid cancer can occur in any age group, although it is most common after age 30 and its aggressiveness increases significantly in older patients. The majority of patients present with a nodule on their thyroid that typically does not cause symptoms.

Occasionally, symptoms such as hoarseness, neck pain, and enlarged lymph nodes do occur. Although as much as 10% of the population will have thyroid nodules, the vast majority are benign. Only approximately 5% of all thyroid nodules are malignant. A nodule that is cold on scan is more likely to be malignant, however, the majority of these are benign as well.

### **Types of Thyroid Cancer and Incidence**

There are four types of thyroid cancer some of which are much more common than others.

- Papillary and mixed papillary/follicular ~78%
- Follicular and Hurthle cell ~ 15%
- Medullary ~5%

- Anaplastic ~ 2%

Most thyroid cancers are very curable. Most common types of thyroid cancer (papillary and follicular) are the most curable. In younger patients, both papillary and follicular cancers can be expected to have better than 95% cure rate if treated appropriately. Both papillary and follicular cancers are typically treated with complete removal of the lobe of the thyroid which harbors the cancer, plus, removal of most or all of the other side. The bottom line, most thyroid cancers are papillary thyroid cancer, and this is one of the most curable cancers of all cancers that humans get.

Medullary cancer of the thyroid is significantly less common, but has a worse prognosis. Medullary cancers tend to spread to large numbers of lymph nodes very early on, and therefore requires a much more aggressive operation than does the more localized cancers such as papillary and follicular. This cancer requires complete thyroid removal plus a dissection to remove the lymph nodes of the front and sides of the neck.

The least common type of thyroid cancer is anaplastic which has a very poor prognosis. It tends to be found after it has spread and is not cured in most cases. Often an operation cannot remove the entire tumor. These patients often require a tracheostomy during the treatment, and treatment is much more aggressive than for other types of thyroid cancer, because this cancer is much more aggressive. (2)

## Stages of Thyroid Cancer

Once cancer of the thyroid is diagnosed, more tests will be done to find out if cancer cells have spread to other parts of the body. This is called staging. You need to know the stage of the disease to plan treatment. The following stages are used for papillary cancers of the thyroid:

- Stage I papillary – Cancer is only in the thyroid and may be found in one or both lobes.
- Stage II papillary – In patients younger than 45 years of age: cancer has spread beyond the thyroid. In patients older than 45 years of age: cancer is only in the thyroid and larger than 1 centimeter (about ½ inch).
- Stage III papillary – Cancer is found in patients older than 45 years of age and has spread outside the thyroid (but not outside of the neck) or has spread to the lymph nodes.
- Stage IV papillary – Cancer is found in patients older than 45 years of age and has spread to other parts of the body, such as the lungs and bones.

The following stages are used for follicular cancers of the thyroid:

- Stage I follicular – Cancer is only in the thyroid and may be found in one or both lobes.
- Stage II follicular – In patients younger than 45 years of age; cancer has spread beyond the thyroid. In patients older than 45 years of age: cancer is only in the thyroid and larger than 1 centimeter (about ½ inch).
- Stage III follicular – Cancer is found in patients older than 45 years of age and has spread outside the thyroid (but not outside of the neck) or to the lymph nodes.
- Stage IV follicular – Cancer is found in patients older than 45 years of age and has spread to other parts of the body, such as the lungs and bones.

Other types or stages of thyroid cancer include the following:

- Stage I medullary – Cancer is less than 1 centimeter (about ½ inch) in size.
- Stage II medullary – Cancer is between 1 and 4 centimeters (about ½ to 1-1/2 inches) in

size.

- Stage III medullary – Cancer has spread to the lymph nodes.
- Stage IV medullary – Cancer has spread to other parts of the body.
- Anaplastic – There is no staging system for anaplastic cancer of the thyroid. This type of cancer of the thyroid grows faster than the other types.
- Recurrent - recurrent disease means that the cancer has come back (recurred) after it has been treated. It may come back in the thyroid or in another part of the body. (3)

The most common system used to describe the stages of cancer is the American Joint Committee on Cancer (AJCC) TNM system. "T" stands for tumor. "N" stands for spread to lymph nodes. "M" is for metastasis. Using the TNM staging system, information about the tumor, lymph nodes, and metastasis is combined to assign a stage, described in Roman numerals from I to IV. This process is called stage grouping. Additional letters or numbers appear after T, N, and M to provide more 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."

The values for T are:

- TX: Primary tumor cannot be assessed
- T0: No evidence of primary tumor
- T1: The tumor is 2 cm (slightly less than an inch) or smaller
- T2: Tumor is between 2 cm and 4 cm (slightly less than 2 inches)
- T3: Tumor is larger than 4 cm or has slightly grown outside the thyroid.
- T4a: Tumor of any size and has grown beyond the thyroid gland to invade nearby tissues of the neck
- T4b: Tumor has grown either back to the spine or into nearby large blood vessels

The values for N are:

- NX: Regional (nearby) lymph nodes cannot be assessed
- N0: No regional lymph node spread
- N1: Spread to lymph nodes
- N1a: Spread to lymph nodes in the neck (cervical lymph nodes)
- N1b: Spread to lymph nodes in the upper chest (upper mediastinal lymph nodes)

The values for M are:

- MX: Presence of distant metastasis cannot be assessed
- M0: No distant metastasis
- M1: Distant metastasis is present, involving nonregional lymph nodes, internal organs, bones, etc.

To make this information clearer, several of these TNM descriptions can be grouped together into stage I through IV. Unlike most other cancers, thyroid cancers are grouped into stages in a way that considers the type of cancer and the patient's age.

All staging systems have found that older people have a greater likelihood of dying from differentiated (papillary or follicular) thyroid cancer. The TNM stage groupings for papillary and follicular carcinomas take this fact into account. So, all people under age 45 years with papillary thyroid cancer, for example, are stage I if they have no distant spread and stage II if they have distant metastases beyond the neck or upper mediastinal lymph nodes.

### **Thyroid Cancer Survival by Stage (5 year relative)**

Stage	Papillary:	Follicular:	Medullary:
<b>I</b>	100%	100%	100%
<b>II</b>	100%	100%	97%
<b>III</b>	96%	79%	78%
<b>IV</b>	45%	47%	24%

Anaplastic: The 5-year relative survival for stage IV anaplastic (or undifferentiated) carcinoma is around 9%.

The 5-year survival rate refers to the percentage of patients who live at least 5 years after their cancer is diagnosed. Five-year rates are used to produce a standard way of discussing prognosis. Of course, many people live much longer than 5 years. Five-year relative survival rates (also called disease-specific) exclude patients dying of other diseases. This means that anyone who died of another cause, such as heart disease, is not counted. Of course, 5-year survival rates are based on patients diagnosed and initially treated more than 5 years ago. Improvements in treatment often result in a more favorable outlook for recently diagnosed patients. (2)

## Facts

- Thyroid cancer is the most common endocrine cancer.
- Thyroid cancer is one of the few cancers that has increased in incidence rates over the past several years. Its incidence has increased by about 3% per 100,000 people per year.
- The American Cancer Society estimates that there will be about 25,690 new cases of thyroid cancer in the U.S. in 2005. Of these new cases, about 19,190 will occur in women and about 6,500 will occur in men. About 1,490 people (860 women and 630 men) will die of thyroid cancer in 2005.
- Many patients, especially in the early stages of thyroid cancer, do not experience symptoms.
- Risk factors associated with thyroid cancer include:
  - A family history of thyroid cancer
  - Gender (women have a higher incidence of thyroid cancer)
  - Age (the majority of cases occur in people over 40, although thyroid cancer affects all age groups from children through seniors)
  - Prior exposure of the thyroid gland to radiation
  - Asian people have an increased risk of developing thyroid cancer
  - Women whose last pregnancy occurs at age 30 or later appear to be at higher risk of thyroid cancer than are women who have children earlier in life
  - White Americans are more likely to develop thyroid cancer than black Americans
- While the prognosis for most thyroid cancer patients is very good, the rate of recurrence can be up to 30%, and recurrences can occur even decades after the initial diagnosis. Therefore, it is important that patients get regular follow-up examinations to detect whether the cancer has re-emerged. Monitoring should continue throughout the patient's lifetime.(3)

## Treatments

There are treatments for all patients with thyroid cancer. Four types of treatment are used:

- Surgery
- Radiation therapy
- Hormone therapy

- Chemotherapy

Surgery is the most common treatment of thyroid cancer. A doctor may remove the cancer with the following operations:

- Lobectomy removes only the side of the thyroid where the cancer is found. Lymph nodes may be biopsied to see if they contain cancer.
- Near-total thyroidectomy removes all of the thyroid except for a small part.
- Total thyroidectomy removes the entire thyroid.
- Lymph node dissection removes lymph nodes in the neck that contain cancer.

Radiation therapy uses high-energy x-rays to kill cancer cells and shrink tumors. Radiation for thyroid cancer may come from a machine outside the body (external radiation therapy) or from drinking a liquid that contains radioactive iodine. Because the thyroid takes up iodine, the radioactive iodine collects in thyroid tissue remaining in the body and kills the cancer cells.

Hormone therapy uses hormones to stop cancer cells from growing. In treating thyroid cancer, hormones can be used to stop the body from making other hormones that might make cancer cells grow. Hormones are usually given as pills. After surgery for thyroid cancer, you'll need to take the thyroid hormone medication levothyroxine (Levothroid, Synthroid) for life. This has two benefits: it supplies the missing hormone the thyroid would normally produce, and it suppresses the pituitary's production of TSH, which signals the thyroid to manufacture hormones. High TSH levels could conceivably stimulate any remaining cancer cells to grow.

Chemotherapy uses drugs to kill cancer cells. Chemotherapy may be taken by pill, or it may be put into the body by a needle in the vein or muscle. Chemotherapy is called a systemic treatment because the drug enters the bloodstream, travels through the body, and can kill cancer cells outside the thyroid.

Other treatments for papillary and follicular cancers include;

- Radioactive iodine (radioiodine) therapy – this therapy may be used in treating thyroid cancer for two reasons. One is to destroy any normal tissue that remains after near-total thyroidectomy. A procedure called remnant ablation uses a moderate dose of iodine to destroy the rims of tissue that have been left after surgery to protect the parathyroids. Radioiodine therapy is a standard treatment for follicular cancer and may sometimes be used in people with papillary cancer. Radioiodine therapy may also be used to destroy any cancer that has spread beyond the thyroid gland. In this treatment, you take a capsule containing iodine 131, usually at a higher dose than is used for remnant ablation. Because iodine 131 is taken up primarily by thyroid tissue, including thyroid cancer cells, other parts of the body are not affected. The patient must have any remaining thyroid tissue removed before he can undergo radioiodine therapy. That is because normal thyroid tissue absorbs more iodine than do cancer cells, and its presence would make the treatment less effective. In addition, you need high blood levels of TSH in order for cancer cells to take up radioactive iodine. For that reason, you normally must discontinue taking thyroid hormones for up to two weeks before therapy.
- External beam radiation – like radioiodine therapy, external beam radiation uses radiation to destroy cancer cells. But in this case, the rays come from a source outside your body – a high-energy x-ray machine called a linear accelerator. The cancer cells are targeted with a high dose of radiation for a few minutes at a time, usually five days a week, over the course of 6-8 weeks. The goal is to destroy the cancer cells while minimizing damage to healthy tissue. The patient is likely to feel very tired later in the course of treatment, and the skin may become red and tender in the treated area. The patient may also feel hoarse or have trouble swallowing.

Treatment of thyroid cancer depends on the type and stage of the disease, and the patient's age and overall health. Standard treatment may be considered because of its effectiveness in patients in past studies, or participation in a clinical trial may be considered. Not all patients are cured with standard therapy and standard treatments may have more side effects than are desired. For these reasons, clinical trials are designed to find better ways to treat cancer patients and are based on the most up-to-date information. (4)

## **Diagnosis**

To help determine whether a nodule is malignant, you may have one or more of the following tests:

- Blood tests – If the doctor suspects medullary cancer, you may have tests that check for high levels of calcitonin in your blood. Other tests can provide information about the function of the thyroid gland.
- Thyroid scan - This was once the primary way of assessing thyroid nodules. During the test, a radioactive isotope is injected into the vein on the inside of the elbow. The patient would then lie on a table while a special camera produces an image of the thyroid on a computer screen. The length of the scan varies, depending on how long it takes the isotope to reach the thyroid gland. The disadvantage of a thyroid scan is that it can't distinguish between malignant and benign nodules. The patient would be exposed to a small amount of radiation during the test.
- Fine-needle aspiration (FNA) biopsy – This test is generally considered the most sensitive for distinguishing between benign and malignant thyroid nodules. During the procedure, the doctor places a thin needle through the skin and into a nodule and removes a sample of cells. Several passes are usually needed to obtain tissue from different parts of the nodule. If there is more than one nodule, the doctor is likely to take samples from as many as possible. Sometimes the doctor may use ultrasound to help guide the placement of the needle. The samples are then sent to a laboratory and analyzed under a microscope. Only a small percentage of biopsied nodules are malignant. This diagnosis is based on the characteristics of individual cells and patterns in clusters of cells that are different from normal thyroid tissue. In some cases, a pathologist can determine specific types of cancer from an FNA biopsy sample.
- Surgical biopsy – occasionally, an FNA doesn't provide a definitive diagnosis. In that case, the doctor may operate to remove the nodule, which is then examined in a pathology laboratory. (5)

## **Thyroid Tests**

The following are commonly used thyroid tests:

- Measurement of Pituitary Production of TSH
- Measurement of Serum Thyroid Hormones: T4 by RIA (radioimmunoassay) – is the most used thyroid test of all.
- Measurement of Serum Thyroid Hormones: T3 by RIA
- Thyroid Binding Globulin
- Iodine Uptake Scan – is a means of measuring thyroid function by measuring how much iodine is taken up by the thyroid gland (RAI uptake).
- Thyroid Scan – two types of thyroid scans are available. A camera scan is performed most commonly which uses a gamma camera operating in a fixed position viewing the entire thyroid gland at once. A Computerized Rectilinear Thyroid (CRT) scanner utilizes computer technology to improve the clarity of thyroid scans and enhance thyroid nodules. It measures both thyroid function and thyroid size. Thyroid scans are used for the following reasons:

- identifying nodules and determining if they are "hot" or "cold"
- measuring the size of the goiter prior to treatment
- follow-up of thyroid cancer patients after surgery
- locating thyroid tissue outside the neck, i.e. base of the tongue or in the chest
- Thyroid Ultrasound – refers to the use of high frequency sound waves to obtain an image of the thyroid gland and identify nodules
- Thyroid Antibodies – the body normally produces antibodies to foreign substances such as bacteria; however, some people are found to have antibodies against their own thyroid tissue. A condition known as Hashimoto's Thyroiditis is associated with a high level of these thyroid antibodies in the blood.
- Thyroid Needle Biopsy – has become the most reliable test to differentiate the "cold" nodule that is cancer from the "cold" nodule that is benign ("hot" nodules are rarely cancerous). It provides information that no other thyroid test will provide. It will provide definitive information in 75% of the nodules biopsied. (3)

## **The Low-Iodine Diet**

Most thyroid cancer patients undergo scans at periodic intervals using a "tracer" dose of radioactive iodine (RAI). If their scan is not "clean", they then undergo a larger dose of RAI in an attempt to destroy any remaining thyroid cells in their bodies. In preparation for the scan many patients are asked to go on a low-iodine diet. This diet is for a short period. The usual time period is around two weeks or slightly more. The point of a low-iodine diet is to deplete the body of its natural stores of iodine that makes the radioactive iodine treatment more effective. The premise is that when the radioactive iodine is administered, the thyroid will "suck" up the iodine because it has been so depleted.

### **The Low-Iodine Diet**

Low iodine has nothing to do with sodium. Sodium in any form is okay as long as it is not provided as 'iodized' salt. Non-iodized salt is okay for the diet. During the time on a low-iodine diet, patients must avoid foods high in iodine (over 20 mcg per serving) and limit foods moderate in iodine (5-20 mcg per serving). The patient may freely eat any foods that are low in iodine (up to 5 mcg) per serving.

The patient must avoid the following foods. These foods and ingredients are high in iodine:

- Iodized salt and sea salt and any foods containing iodized salt or sea salt. All products from the ocean tend to be high in iodine.
- Seafood and sea products (seaweed, kelp, fish, shellfish)
- Dairy products. Non-dairy creamers often have iodine-containing ingredients too.
- Egg yolks or whole eggs or foods containing whole eggs. Egg whites are acceptable, because they do not contain iodine.
- Foods or products that contain these additives: carrageen, agar-agar, algin, alginate, and nori (these are food additives that are seaweed by-products).
- Commercial bakery products.
- Red Dye #3. However, Red Dye #40 is okay.
- Chocolate (for its milk content).
- Molasses (sulfured).
- Soy products – these vary in iodine content.
- Some beans – avoid red kidney beans, lima beans, navy beans, pinto beans, and cowpeas.
- Potato skins – these have iodine.
- Rhubarb.
- Iodine-Containing Vitamins, and Food Supplements – most vitamins with minerals contain



iodine. (6)

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## Course Exam

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1. Men have a higher incidence of thyroid cancer.  
 True  False
2. White Americans are more likely to develop thyroid cancer than black Americans.  
 True  False
3. In the TNM staging system, 'T' stands for time.  
 True  False
4. Thyroid cancer is the most common endocrine cancer.  
 True  False
5. Stage III papillary cancer is only in the thyroid and may be found in one or both lobes.  
 True  False
6. The thyroid gland is under the control of the pituitary gland.  
 True  False
7. Common symptoms of thyroid cancer may include a lump in the neck, a pain in the neck, hoarseness and trouble swallowing.  
 True  False
8. There are four types of thyroid cancer.  
 True  False
9. There are over 37,000 new cases of thyroid cancer each year in the U.S.  
 True  False

10. Of the types of thyroid cancer, papillary and mixed papillary/follicular equal about 78% of the cases.
- True  False
11. Most thyroid cancers are not curable.
- True  False
12. The least common type of thyroid cancer is anaplastic which has a very poor prognosis.
- True  False
13. The normal thyroid gland produces about 80% T3 and about 20% T4.
- True  False
14. In Stage III medullary, cancer has spread to the lymph nodes.
- True  False
15. The function of the thyroid gland is to make iodine.
- True  False
16. In the TNM staging system, the letter "X" means "cannot be assessed because the information is not available."
- True  False
17. The 5-year relative survival for stage IV anaplastic carcinoma is around 9%.
- True  False
18. T3 possesses about four times the hormone 'strength' as T4.
- True  False
19. The thyroid gland is a small gland normally weighing about five ounces.
- True  False
20. The thyroid is situated just below the 'Adams apple' or larynx.
- True  False