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Thyroid Cancer

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These NCCN Guidelines for Patients are based on the NCCN Guidelines® for Thyroid Carcinoma (Version 2.2020, July 15, 2020).

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The American Thyroid Association® (ATA) is pleased to endorse the NCCN Guideline for Patients: Thyroid Cancer in support of, our mutual goal of expanding patients' access and awareness of thyroid cancer treatment guidelines and resources. thyroid.org

The THANC Foundation

The THANC Foundation is pleased to endorse this valuable resource. We believe this comprehensive guide will help patients understand and prepare for every step of the thyroid cancer journey. thancfoundation.org

Head and Neck Cancer Alliance

HNCA's mission is to advance prevention, detection, treatment and rehabilitation of oral, head and neck cancer through public awareness, research, advocacy and survivorship. HNCA's programs include peer-to-peer mentorship, online support community, educational information, Awareness Week, survivorship resources, an Ambassador program, and more. Visit headandneck.org or call 866-792-HNCA (4622) for more information

Thyroid Care Collaborative

The Thyroid Care Collaborative organization strongly endorses this valuable resource. We believe this comprehensive guide will ensure patients are well-informed - an important step to the fight against thyroid cancer! thyroidccc.org

Support For People With Oral And Head And Neck Cancer (SPOHNC)

A non-profit organization involved in the development of programs of support. As such it can have an enormous positive impact on meeting the psychosocial needs of patients as well as preserving, restoring and promoting physical and emotional health. SPOHNC is dedicated to raising awareness and meeting the needs of oral and head and neck cancer patients through its resources and publications. Visit SPOHNC at spohnc.org to become empowered with the essential programs and resources. Together We Heal!

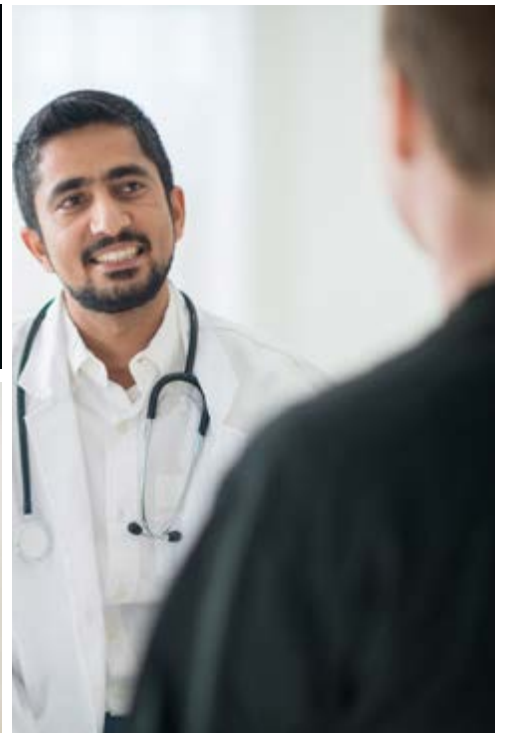
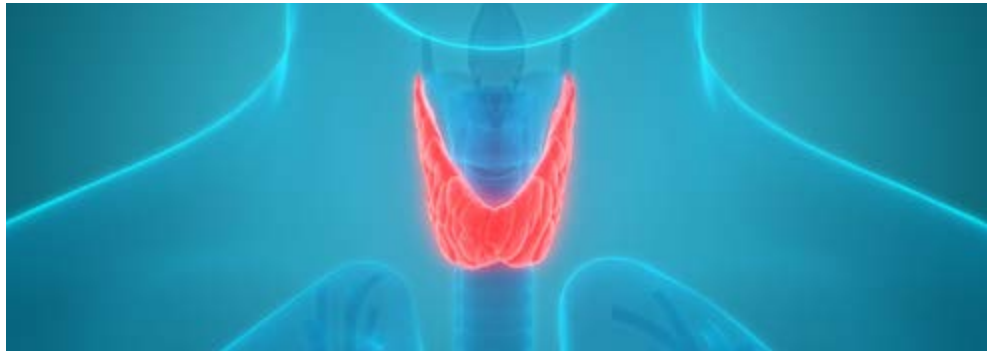
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Thyroid Cancer Survivors' Association, Inc. is proud to collaborate with the National Comprehensive Cancer Network to endorse the NCCN Guidelines for Patients: Thyroid Cancer. thyca.org

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Thyroid cancer basics

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Several different types of cancer can start in the thyroid gland. Most are curable with the right treatment. Surgery is needed for almost all thyroid cancers.

The thyroid

The thyroid is a gland in the front of the neck, below the Adam's apple. It makes substances called hormones that are essential for the body to function properly. These hormones circulate in the blood and help regulate body temperature, blood pressure, heart rate, weight, and metabolism (how fast food becomes fuel for your body). The thyroid uses a mineral from your diet called iodine to produce these hormones. Certain foods and iodized salt contain iodine.

The two main hormones made by the thyroid are triiodothyronine (T3) and thyroxine (T4).

Together, these are often referred to simply as “thyroid hormone.”

Structure of the thyroid

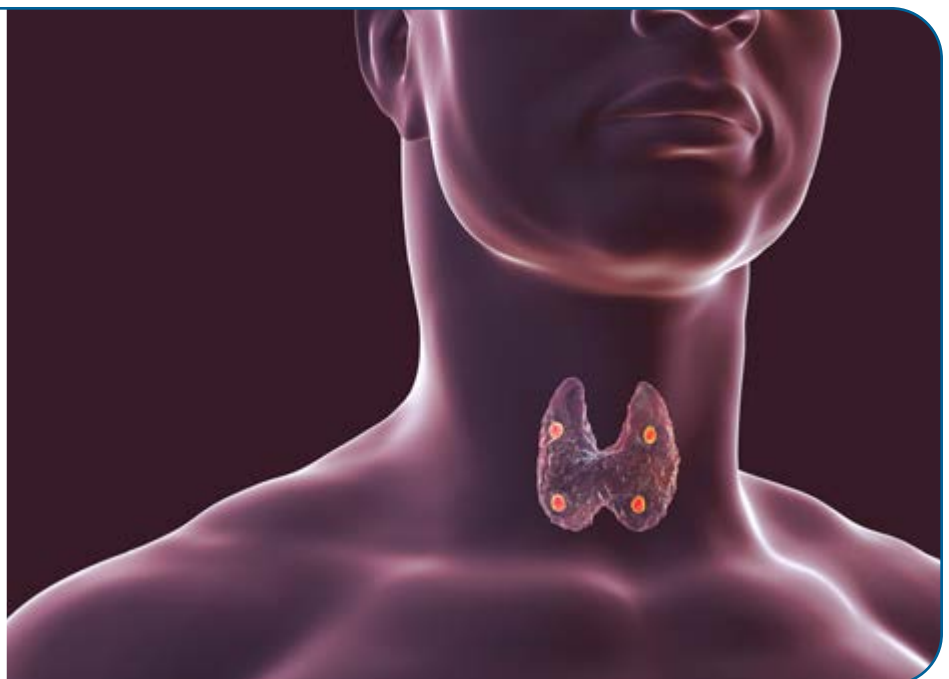
The thyroid is butterfly-shaped. It has two lobes, a right and a left. A thin piece of tissue called the isthmus connects the two lobes. There are four pea-sized glands in the neck, behind the thyroid gland. These are known as the parathyroid glands. They control the amount of calcium in your bloodstream.

Thyroid nodules

Thyroid nodules are small, often round areas of atypical tissue. Most are not cancerous. Very small nodules usually can't be seen or felt, but a large nodule may be found during a hand examination of the neck.

Thyroid gland

The thyroid is a butterfly-shaped gland in the lower, front part of the neck. It makes hormones that control body functions including blood pressure and metabolism.



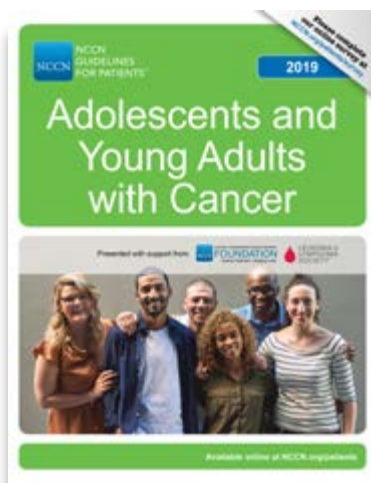
Most thyroid nodules do not cause symptoms. They are often found by imaging tests done for a different reason. Possible symptoms of larger nodules include:

- A noticeable lump in the neck
- Neck pain
- Voice changes
- Trouble breathing
- Problems swallowing

Who is at risk?

Women are 3 times more likely than men to develop a thyroid cancer. Compared to other cancers, thyroid cancer is often diagnosed earlier in adulthood. It is the most common cancer in young adults ages 18 to 33.

See *NCCN Guidelines for Patients: Adolescents and Young Adults with Cancer* at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines).



Anything that increases the chances of getting a disease is called a risk factor. The most well-known risk factors for thyroid cancer are radiation exposure and a family history of thyroid cancer.

Radiation exposure

Anyone who has had treatment with head or neck radiation in the past (to treat a childhood cancer, for example) is at increased risk of thyroid cancer. Contact with large amounts of radiation in the environment as a result of a catastrophic event also increases the risk of developing a thyroid cancer.

Family history

Most thyroid cancers are sporadic, meaning there is no clear risk factor. In some cases, however, thyroid cancer can be hereditary.

A personal or family history of thyroid cancer or a related syndrome may increase the risk of thyroid cancer. Syndromes related to thyroid cancer include familial adenomatous polyposis (FAP), Carney complex, Cowden syndrome, and multiple endocrine neoplasia (MEN).

An increased risk for certain cancers can be passed from parents to children through genes. A process called mutation is when a change occurs in the genetic code. Mutations can be passed on from a parent and present before you are born (inherited), or they can be caused by genetic damage (acquired) that occurs later in life.

People with inherited genetic mutations have a higher risk for certain cancers, but will not always develop the cancer. Only a small number of thyroid cancers are a result of inherited mutations.

Prognosis

Prognosis refers to the expected course or outcome of a disease. This includes how likely the cancer is to be cured and how likely it is to return. Most thyroid cancers have an excellent prognosis, especially if found before age 55.

Testing for thyroid cancer

Although most nodules are not cancerous, testing is recommended if a nodule is found.

First tests

The first tests usually ordered after a thyroid nodule is discovered or suspected are:

- Thyroid-stimulating hormone (TSH) blood test
- Ultrasound of the thyroid and neck

TSH test

TSH is a hormone made by the pituitary gland, located near the base of the brain. TSH controls the hormones made by the thyroid. The TSH level can fluctuate for reasons other than cancer. For this reason, a TSH blood test alone cannot diagnose thyroid cancer. However, when combined with ultrasound results, the TSH level can help determine whether a biopsy is needed.

A high TSH level usually means that the thyroid hormone levels are low. Likewise, a low TSH level usually means that the thyroid hormone levels are high. If the TSH is low (which may suggest overactive thyroid), your doctor may order a radioiodine (RAI) uptake test.

Ultrasound

Ultrasound is the most common imaging technique used to look for thyroid cancer. It uses sound waves to form images showing the size, shape, and location of a thyroid nodule. An ultrasound of the thyroid and neck is brief and painless. It is usually done lying down. A hand-held device called an ultrasound probe is used. After a gel is applied to the skin, the probe is moved back and forth over the thyroid area.

Currently, there is no screening test for thyroid cancer. Screening is testing for a disease in someone without symptoms.

Although ultrasound is used most often, the following imaging tests may be used in certain situations:

- Computed tomography (CT)
- Positron emission tomography (PET)
- Magnetic resonance imaging (MRI)

Biopsy

A biopsy removes samples of fluid or tissue from the body to be tested. Your doctor will consider the nodule size and other features as seen on the ultrasound exam to determine if a biopsy is needed. Some nodules do not need to be biopsied and are monitored with ultrasound.

If a biopsy is needed, the type used most often for thyroid cancer is called fine-needle aspiration (FNA). FNA is often referred to simply as a “needle biopsy.” FNA uses a thin needle to take small samples of suspicious thyroid nodules. Ultrasound is usually done at the same time to help pinpoint the suspicious areas.

Pathology review

The biopsy samples are sent to a pathologist. Pathologists are physicians with expertise in examining tissues and cells to diagnose disease. By examining the sample under a microscope, the pathologist determines whether the nodule is cancerous, and if so, the cancer type. In certain types of lesions, such as follicular and Hürthle cell tumors, FNA can identify the nature of the cells, but cannot determine if the nodule is benign or malignant. In these lesions, surgery is needed to make a final diagnosis. In recent years, molecular tests have been developed to help decide if surgery is necessary when the biopsy results cannot determine whether the nodule is cancerous or benign.

Papillary carcinoma is the most common type of thyroid cancer, followed by follicular carcinoma. Papillary, follicular, and Hürthle cell carcinomas are known as the “differentiated”

thyroid cancers. Differentiated cancers usually grow and spread slowly. Treatment of these types is addressed in the following chapter.

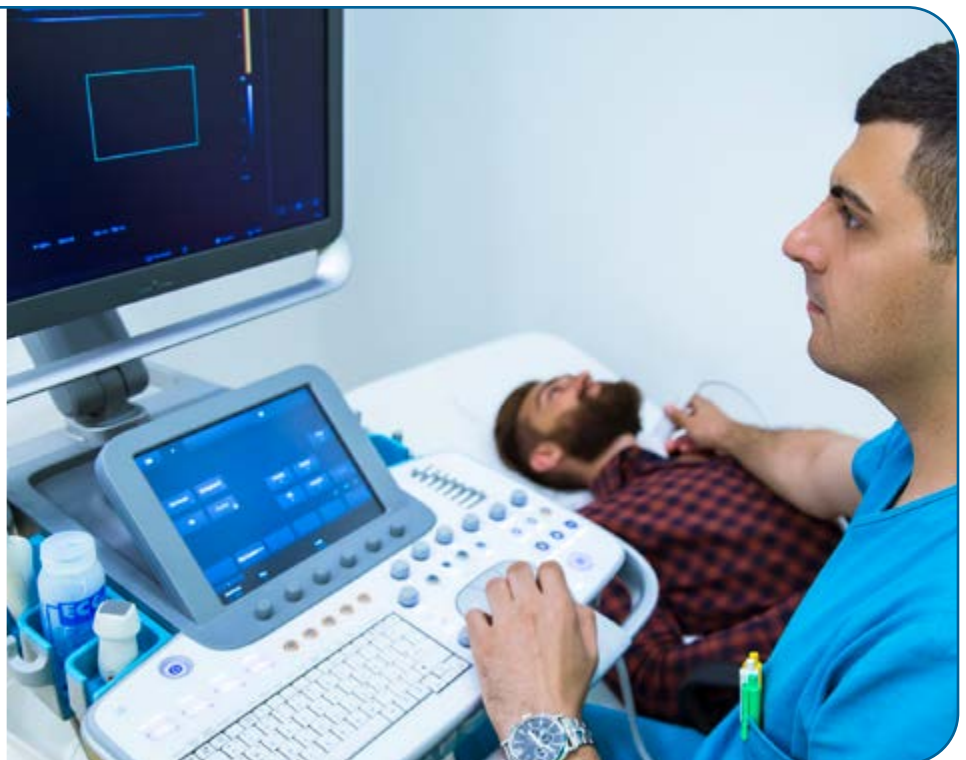
Medullary thyroid cancer is the third most common type, after papillary and follicular. This type can be inherited, meaning it can run in families. Medullary thyroid cancer is the focus of chapter 3, beginning on page 29.

Anaplastic thyroid cancer is the most aggressive type of thyroid cancer. It is rare and most often affects older adults. This type is the focus of chapter 4, beginning on page 36.

The type and other features of benign and malignant lesions are recorded in a pathology report. You are encouraged to request a copy of the report for your reference and to have for your records. It is used by your treatment team to plan further testing and treatment.

Ultrasound

An ultrasound of the thyroid and neck is one of the first tests ordered if a thyroid nodule is known or suspected.



Treatments for thyroid cancer

Surgery (described next) is the most common treatment for almost all thyroid cancers. However, active surveillance may be an option for some very low risk thyroid cancers. This involves careful monitoring of the cancer instead of doing surgery right away.

Surgery

Surgery is the most effective treatment for thyroid cancer. Surgery may involve removing the entire thyroid gland, or just the half with cancer.

Lobectomy

A lobectomy removes the lobe of the thyroid that contains the cancerous nodule (the tumor). The tissue connecting the two lobes (the isthmus) is also removed. While under general anesthesia, a small incision is made in the front of the neck to remove the cancerous lobe. Lobectomy may be an option for some small and low-risk differentiated thyroid cancers.

Total thyroidectomy

A total thyroidectomy removes the entire thyroid gland. While under general anesthesia, a small incision is made in the front of the neck to remove the gland. Lymph nodes near the thyroid are also removed if they are known or suspected to have cancer. This is called a neck dissection.

A neck dissection may also be done in order to treat or relieve symptoms caused by the lymph nodes, or to prevent the spread of cancer through lymph nodes. Other tissue in the neck may be removed during a neck dissection.



Treatment team

Treating thyroid cancer takes a team of experts. Your treatment team may include an endocrinologist, radiologist, nuclear medicine specialist, surgeon, radiation oncologist, and medical oncologist.

Your treatment team will work together to decide on the treatment plan that is best for you. A treatment plan is a written course of action that covers every phase of the treatment process.

Side effects

With any surgery, there is risk of infection, bleeding, or pain. Your treatment team can give you a complete list of side effects. Most people stay in the hospital for a few days after surgery. After being discharged, it is important to follow the instructions for at-home care. Contact your care team about any new or worsening side effects.

Possible long-term side effects of removing the thyroid include:

- Low levels of calcium in the blood (hypoparathyroidism)
- Damage to the nerves that control your voice and swallowing

Thyroid hormone replacement therapy

After a total thyroidectomy, medicine is used to replace the hormones no longer being supplied by the thyroid. This is called thyroid hormone replacement therapy. It is needed lifelong after total thyroidectomy. After a lobectomy, about 1 in 5 people need thyroid hormone replacement.

Levothyroxine (eg, Levoxyl[®]; Synthroid[®]) is the most commonly used thyroid hormone replacement therapy. The goal for most patients is to keep the level of thyroid-stimulating hormone (TSH) in the low normal range. For higher risk thyroid cancers, or if there are signs of recurrence, the TSH level is kept lower than the normal range (“suppressed”). This helps prevent thyroid cancer cells from growing or returning.

Levothyroxine is taken as a pill once a day. Common side effects if the dose of levothyroxine isn’t optimal include:

- Sweating
- Anxiety
- Trouble sleeping

Determining the right dose of levothyroxine can take some trial and error. Too much levothyroxine can cause health problems, including:

- Weakened bone strength
- Heart rhythm problems
- Having too much thyroid hormone (thyrotoxicosis)

Blood tests are used to check the TSH on a regular basis during thyroid replacement therapy. Your doctor can find the right dose of thyroid hormone for you by checking the TSH level and adjusting the dose as needed.

Calcium and vitamin D

Your care team may recommend taking calcium and vitamin D supplements to help strengthen bones.

Radioactive iodine therapy

Radioactive iodine (RAI) therapy uses radiation to selectively kill cancer cells that take up (“eat”) iodine. RAI therapy targets cancerous thyroid cells in the neck and elsewhere in the body. The goal is to treat only the thyroid cells and avoid harming healthy tissue. RAI therapy uses a form of radioactive iodine called iodine-131 that destroys thyroid cells. RAI therapy may be used in the following situations:

- To reduce the risk of recurrence in higher-risk thyroid cancers
- To treat known metastatic disease
- Shortly after thyroidectomy for lower-risk cancer using lower-dose iodine-131 (also known as remnant ablation)

RAI therapy is used after total thyroidectomy for differentiated thyroid cancers that take up iodine. Most papillary and follicular thyroid cancers take up iodine. Hürthle cell thyroid cancer may take up iodine less often. RAI is not effective against medullary or anaplastic thyroid cancer. RAI therapy is generally only recommended for those at higher risk of cancer recurrence.

How is it given?

RAI therapy comes in liquid or pill form and is taken by mouth. You may be asked to eat a diet low in iodine for 1 to 2 weeks before starting this treatment. Hormone injections may be given to increase the TSH level several days before RAI is started. Or, thyroid hormone replacement may be stopped for several weeks before RAI therapy.

Possible side effects of RAI therapy include:

- Neck pain or swelling
- Nausea and vomiting
- Dry mouth or eyes
- Watery eyes
- Change in taste or smell

If you have a CT scan with contrast, it can delay the start of treatment with RAI therapy. Your doctor will consider this when planning your care. A CT may be necessary to see more of the neck or chest area to check for disease.

The dose of RAI therapy is adjusted for children with thyroid cancer and people on dialysis for kidney disease. If any cancer can be removed by surgery, this will be considered before starting RAI therapy.

Safety measures

The radiation itself will exit your body through urine and other body fluids. This means that your body will give off small amounts of radiation after treatment. For a short period, you will need to take safety measures around other people, especially children or pregnant women. Ask your care team for a complete list of instructions on your care before, during, and after RAI therapy.

Whole-body RAI scan

After RAI therapy, a whole-body radioiodine scan is performed to look for remaining thyroid tissue and “hidden” areas of thyroid cancer in the body. At some treatment centers, a whole-body scan is also done before RAI therapy. This imaging can be done using small doses of iodine-131 or larger doses of a similar form of radioactive iodine called iodine-123.

A whole-body RAI scan is often done when thyroid hormone replacement therapy is paused. If stopping thyroid hormone is not recommended, there is another option for doing the scan. A medication known as thyrotropin alfa (Thyrogen®) can be used. Thyrogen activates iodine uptake so that hormone replacement with levothyroxine can be continued during imaging and therapy.

Targeted therapy

Targeted therapies are medicines that can target and attack specific types of cancer cells. Targeted therapy is generally only used for thyroid cancers that:

- Cannot be treated with surgery or RAI therapy
- Have returned after treatment (recurred)
- Have spread to areas far from the neck (metastasized) and are continuing to grow

The targeted therapies currently used for thyroid cancer are known as kinase inhibitors. The recommended kinase inhibitors differ somewhat by thyroid cancer type. See the chapters that follow for the targeted therapies used for a specific type of thyroid cancer.

Side effects of targeted therapy may include:

- Tiredness (fatigue)
- Body aches
- Rash
- Not wanting to eat
- Nausea and vomiting
- Diarrhea
- Constipation
- Low blood cell counts
- High blood pressure
- Abnormal bleeding

Because targeted therapy does not harm normal cells as much as chemotherapy, the side effects tend to be less severe.

Some targeted therapies have serious side effects that can affect your heart, skin, and digestive system. If targeted therapy is planned, ask your treatment team for a complete list of potential side effects. Tell your treatment team about any new or worsening side effects.

Radiation therapy

Radiation therapy uses high-energy rays to destroy small areas of cancer. In the treatment of thyroid cancer, radiation is given using a large machine outside the body. This is called external radiation therapy.

The use of radiation therapy differs by thyroid cancer type. It is rarely used for papillary and follicular cancers. Anaplastic thyroid cancer, in contrast, is almost always treated with radiation therapy.

Radiation therapy may be used for thyroid cancer that cannot be removed with surgery and does not respond to RAI therapy. Radiation therapy can also relieve symptoms caused by cancer. For thyroid cancer that has spread, this could include difficulty or pain swallowing, loss of your voice, or pain or stiffness in your neck.

Radiation therapy plan and schedule

You will first have a planning session called a simulation. You will be placed in the treatment position and a CT scan will be done. The CT scan images will be used to make your radiation plan. The plan will describe the best radiation dose for you, as well as the number of sessions that are needed.

During radiation treatment, you will lie on a table in the same position as done during simulation. Devices may be used to keep you from moving so that the radiation targets the tumor. You will be alone while the technician

operates the radiation machine from a nearby room. He or she will be able to see, hear, and speak with you at all times. One treatment session can take between 30 to 60 minutes. It is common to have 5 sessions per week.

Although the rays target areas of cancer directly, nearby normal cells can also be harmed. Damage to normal cells causes side effects. Common side effects of radiation to the neck area include:

- Skin rash or redness
- Problems swallowing
- Dry mouth
- Tiredness (fatigue)

While most side effects of radiation therapy start when treatment starts and stop when it is over, some can occur years later.

Chemotherapy

Chemotherapy is the use of powerful medicines to treat cancer cells throughout the body. Chemotherapy does not work well against most thyroid cancers. It may be used to treat thyroid cancer that is not responding to other treatment, or that has spread to distant areas of the body. It is most often used for the least common and most aggressive type—anaplastic thyroid cancer.

Most chemotherapy medicines are put directly into the bloodstream through a vein. Chemotherapy is given over a predetermined

Radiation therapy

Radiation therapy uses high-energy radiation from x-rays, gamma rays, protons, and other sources to kill cancer cells and shrink tumors. It is also used to treat pain caused by cancers.



period of time according to established doses and schedules.

Common side effects of chemotherapy include:

- Tiredness (fatigue)
- Nausea and vomiting
- Diarrhea
- Constipation
- Hair loss
- Mouth sores
- Not wanting to eat
- Low blood cell counts

Not all side effects are listed here. If chemotherapy is planned, ask your care team for a complete list. While most side effects start when treatment starts and stop when it is over, some can occur years later. Long-term side effects of chemotherapy can include other

cancers, heart disease, and not being able to have children (infertility).

Clinical trials

A clinical trial is a type of research study that people choose to take part in. Clinical trials help doctors and scientists learn how to prevent, identify, and treat cancer. Because of clinical trials, doctors find safe and helpful ways to improve cancer care.

Clinical trials go through levels or phases of testing. These phases help move the research along to find out what works best for patients with cancer.

- Phase I looks at how much drug to give, its side effects, and how often to give the treatment.
- Phase II tests for side effects and how it works on the cancer type.

Clinical trials

A clinical trial is a type of research study that people choose to take part in. Talk to your care team about whether joining a clinical trial makes sense for you.



- Phase III compares the new treatment (or new use of treatment) to what is commonly used.
- Phase IV follows late side effects and if the treatment still works after a long period.

treatment centers nearby. You can also find clinical trials through the websites listed in the last chapter of this book.

All clinical trials have a plan and are carefully led by a medical team. Patients in a clinical trial are often alike with their cancer type and general health. You can join a clinical trial when you meet certain terms (eligibility criteria).

If you decide to join a trial, you will need to review and sign an informed consent form. This form describes the clinical trial in detail, including the possible risks and benefits. Signing this form does not require that you stay in the clinical trial. You can choose to leave the trial at any time.

Potential benefits of joining a clinical trial include:

- Access to the most current cancer care
- Close monitoring by a team of experts
- Helping other patients with cancer

Potential drawbacks of joining a clinical trial include:

- The test or treatment doesn't help your cancer
- The side effects of the test or treatment are unknown
- More frequent visits to your treatment center

Ask your care team if a clinical trial may be an option for you. There may be clinical trials where you're getting treatment or at other

Review

- The thyroid is a butterfly-shaped gland in the neck. It makes hormones that help regulate metabolism and other body functions.
- Thyroid cancers start as small, often round areas of atypical tissue called nodules.
- Although most nodules are not cancerous, a TSH test and ultrasound are recommended if a thyroid nodule is known or suspected.
- The TSH and ultrasound results determine whether fine-needle aspiration (FNA) is needed.
- Biopsy samples are sent to a pathologist. The pathologist determines whether the nodule is cancerous and if so, the cancer type.
- Surgery is the main treatment for thyroid cancer.
- RAI therapy may be used after total thyroidectomy to kill any remaining cancer cells.
- Thyroid hormone replacement therapy with levothyroxine is needed lifelong after total thyroidectomy. About 1 in 5 people need hormone replacement therapy after a lobectomy.
- Targeted therapy may be an option for thyroid cancers that do not respond to other treatments, or that have metastasized and are continuing to grow.
- Chemotherapy is used most often for anaplastic thyroid cancer. It is rarely used to treat other types of thyroid cancer.
- Clinical trials help doctors learn how to prevent, diagnose, and treat cancer and other diseases.
- Your treatment team may include an endocrinologist, radiologist, nuclear medicine doctor, surgeon, radiation oncologist, and medical oncologist.

2

Papillary, follicular, and Hürthle cell

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Papillary, follicular, and Hürthle cell carcinoma are known as differentiated thyroid cancers. These cancers usually grow slowly and have good treatment outcomes.

The differentiated thyroid cancers are treated with surgery to remove all or part of the thyroid. For many years, total thyroidectomy was the standard treatment for all thyroid cancers. Today, it remains a treatment option for everyone with thyroid cancer. However, newer research shows that lobectomy may be just as effective for treating many small, low-risk cancers that have not grown or spread beyond the thyroid. A potential benefit of lobectomy is that thyroid hormone replacement therapy with levothyroxine may not be needed. Or, a lower dose may be needed.

Papillary thyroid cancer

Papillary is the most common of all the thyroid cancers. There are different types of papillary cancer (“subtypes”). The most common subtype is “classic type” papillary thyroid cancer.

Other subtypes that may grow and spread more quickly include:

- Poorly differentiated
- Tall-cell
- Columnar
- Hobnail
- Diffuse sclerosing

Testing

If a needle biopsy diagnoses papillary thyroid cancer, more testing is needed to learn the extent of the cancer before surgery. An ultrasound of the thyroid and front and sides of the neck is recommended, if one hasn’t already been done.

Additional testing may include:

- CT/MRI with contrast
- Vocal cord exam
- Biopsy of suspicious lymph nodes in the neck

Is surgery always needed?

Some small papillary tumors (no bigger than a pea) may be safely monitored without surgery. Monitoring may be an option if:

- There are no nearby lymph nodes suspicious for cancer, and
- The tumor is not in a high-risk location (for example, at the back of the thyroid, butting up against the trachea)
- The tumor is less than 1 centimeter

Thyroidectomy or lobectomy?

Some papillary cancers should always be treated with total thyroidectomy. A total thyroidectomy is recommended if:

- The cancer has spread to distant areas of the body (metastasized), or
- The cancer has grown beyond the thyroid into the neck, or
- The tumor is bigger than 4 centimeters (about the size of a walnut), or

- The cancer has spread to nearby lymph nodes, or
- It is a high-risk type of papillary cancer.

There are other reasons a total thyroidectomy may be recommended by your treatment team. Factors such as whether the neck area was ever treated with radiation therapy will be considered. Any lymph nodes near the thyroid that are known to have cancer will also be removed during a total thyroidectomy.

If the cancer is small and noninvasive, lobectomy may be a treatment option in addition to thyroidectomy. Lobectomy may be an option if:

- You've never had radiation therapy, and
- The cancer has not spread at all beyond the thyroid, and
- The tumor is smaller than 4 centimeters (about the size of a walnut).

The extent of the cancer can't be fully known until the surgeon sees the thyroid, tumor, and surrounding areas first-hand. If the cancer is larger or more invasive than expected during a lobectomy, the decision is usually made during surgery to remove the entire thyroid.

After thyroidectomy

If the results of surgery are very good, RAI therapy may be used to kill cancer cells left in the body. See page 23 for more information on RAI therapy and next steps of care.

If a concerning amount of cancer remains after surgery, treatment options may include:

- Another surgery

- RAI therapy
- Radiation therapy
- Systemic therapy
- Monitoring

After treatment with one or more of the above, thyroid hormone replacement therapy with levothyroxine is started. Hormone replacement therapy keeps the TSH level down. See *Monitoring and follow-up care* on page 24 for information on next steps.

After lobectomy

After a lobectomy, everything that was removed or sampled (biopsied) during surgery is examined and tested. If testing of the tumor, other tissue, or lymph nodes finds any concerning or high-risk features, another surgery to remove the rest of the thyroid is recommended.

If the results of surgery and testing are very good and no high-risk features are found, more surgery is not usually needed.

The levels of thyroglobulin and anti-thyroglobulin antibodies in the blood may be tested 6 to 12 weeks after surgery. Your doctor may recommend thyroid hormone replacement therapy with levothyroxine. This is on a case-by-case basis. Because the thyroid continues to make hormones after a lobectomy, hormone replacement therapy is not always needed.

➡ See *Monitoring and follow-up care* on page 24 for information on next steps.

Follicular and Hürthle cell

After papillary, follicular is the next most common type of thyroid cancer. Hürthle cell carcinoma is uncommon and more aggressive than the other differentiated thyroid cancers. It has often spread to nearby lymph nodes by the time it is diagnosed. Follicular and Hürthle cell thyroid cancers are known for invading blood vessels in and around the thyroid.

Unlike papillary thyroid cancer, follicular and Hürthle cell cancers cannot be diagnosed with a needle biopsy alone. FNA can only suggest these types. In order to be diagnosed as follicular or Hürthle cell, the thyroid tumor must have grown into blood vessels (eg, veins or arteries) in and around the thyroid or into the protective outer layer of the thyroid (the capsule). This can be learned by removing all or part of the thyroid or in some cases with genetic testing of the biopsy sample.

Thyroidectomy or lobectomy?

A total thyroidectomy is recommended for suspected follicular or Hürthle cell cancers that have grown through the thyroid into the neck (invasive), or have spread to areas far from the thyroid (metastatic). There are other reasons a total thyroidectomy may be recommended by your treatment team.

If the cancer is noninvasive and nonmetastatic, lobectomy may be a treatment option in addition to thyroidectomy. The extent of the cancer can't be fully known until the surgeon sees the thyroid, tumor, and surrounding areas first-hand. If the cancer is more invasive than expected during a lobectomy, the decision is usually made during surgery to remove the entire thyroid.

After thyroidectomy

After surgery, everything that was removed or sampled (biopsied) is examined and tested. Testing may find that the tumor is benign (not cancer). In this case, no more cancer treatment is needed. Lifelong thyroid hormone replacement therapy is needed, however.

If testing confirms follicular or Hürthle cell thyroid cancer, further treatment depends on the results of surgery. If the results of surgery are very good, RAI therapy may be used to kill cancer cells left in the body. RAI therapy is discussed on the next page.

If a concerning amount of cancer remains after surgery, there is more than one possibility. Options may include:

- Another surgery (preferred, if possible)
- RAI therapy
- Radiation therapy
- Systemic therapy
- Monitoring

After treatment with one or more of the above, hormone replacement therapy with levothyroxine is started. Hormone replacement therapy keeps the TSH level down.

➡ See *Monitoring and follow-up care* on page 24 for next steps of care.

After lobectomy

Depending on the extent of cancer observed during surgery, you may have more surgery to remove the rest of the thyroid. If the cancer is invasive, removing the rest of the thyroid is recommended.

For less invasive, or minimally invasive, cancer, surgery to remove the rest of the thyroid is one option. An alternative is to take a watch-and-wait approach and monitor the cancer. If this option is planned, you may receive levothyroxine to keep your TSH level low or normal. This is on a case-by-case basis. Because the thyroid continues to make hormones after a lobectomy, hormone replacement therapy is not always needed.

If the nodule removed during lobectomy is benign, monitoring is recommended. You may receive levothyroxine to keep your TSH level low or normal.

If your doctor suspects (or knows) that the cancer has spread to areas far from the thyroid (metastasized), testing is needed to investigate. Testing typically includes imaging procedures to see the distant areas of cancer (metastases). Whole-body radioiodine scan, positron emission tomography (PET), computed tomography (CT), or magnetic resonance imaging (MRI) are commonly used.

➔ See *Monitoring and follow-up care* on page 24 for next steps of care.

Radioactive iodine therapy

If all or most of the cancer was removed during total thyroidectomy, RAI therapy may be an option to kill thyroid cancer cells left in the body after surgery.

A number of factors are considered in order to decide if RAI therapy may be helpful, including:

- The size of the tumor
- The tumor subtype
- Whether the cancer invaded lymph or blood vessels
- Whether the cancer has spread to lymph nodes
- The thyroglobulin level after surgery
- Age at diagnosis

RAI therapy is generally recommended if:

- The cancer had spread significantly beyond the thyroid
- The original tumor was over 4 centimeters (about the size of a walnut)
- The cancer had invaded blood vessels (applies to follicular and Hürthle cell)
- The thyroglobulin level after surgery was high
- There were large, or more than 5, lymph nodes with cancer

If RAI therapy is planned, you may first have another surgery to remove as much of the remaining cancer as possible. After RAI, a whole-body RAI scan is done to see how well the therapy worked. After RAI, hormone replacement therapy with levothyroxine is

started. The next section, *Monitoring and follow-up care*, provides information on next steps.

Monitoring and follow-up care

A physical examination and blood tests are recommended at 6 months and 1 year after treatment. If the results are normal, these tests are generally only needed once a year going forward.

Blood tests

The blood tests will measure the levels of the following:

- Thyroid-stimulating hormone (TSH)
- Thyroglobulin (Tg)
- Anti-thyroglobulin antibodies

Thyroid hormone is stored in the thyroid as Tg. After removing the thyroid, there shouldn't be any thyroid hormone in the blood. If a blood test detects Tg after a total thyroidectomy, it means there may be thyroid cancer cells in the body.

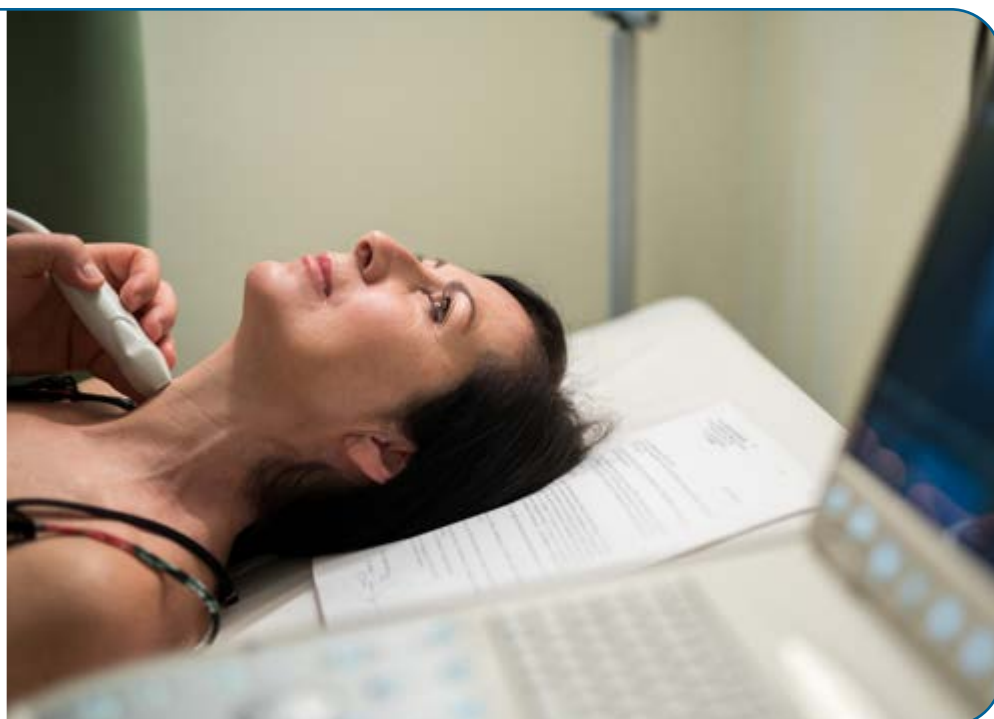
A small number of people with thyroid cancer make antibodies in response to thyroglobulin. These “anti-Tg antibodies” in blood can interfere with the Tg level. If the anti-Tg antibody level goes down, it may be a sign that treatment is working. If it goes up, further testing should be done to check for cancer recurrence.

Ultrasound

Neck ultrasound is also used to monitor for the return of thyroid cancer. Everyone may have ultrasounds at different intervals after treatment. There isn't a one-size-fits-all schedule. Talk to your care team about how often is right for you. Some people at low risk of recurrence may only

Ultrasound

Neck ultrasound is used to monitor for the return of thyroid cancer. Talk to your care team about how often you need to have ultrasounds.



need an ultrasound if there is reason to suspect the cancer has returned.

RAI imaging

Whole-body RAI imaging is used in some cases to look for cancer after treatment. It may be helpful for:

- High-risk patients
- Patients who had metastases that took up iodine
- Abnormal blood test or ultrasound results

Long-term monitoring

If follow-up test results continue to be normal, it is considered no evidence of disease (NED). In very low-risk patients with NED, long-term surveillance may include:

- Yearly thyroglobulin testing without stopping thyroid hormone, and
- Periodic neck ultrasounds.

If there is reason to suspect the cancer has returned, you may have TSH-stimulated testing (testing while thyroid hormone is stopped) or imaging procedures such as CT or MRI.

If cancer comes back

Although the thyroid has been removed, cancer can return to the neck or to areas far from the neck. The return of cancer after treatment is called recurrence.

Thyroglobulin (Tg) blood tests are used to determine whether there are cancer cells in the body after surgery and RAI therapy.

If the thyroglobulin level is slightly high but there are no signs of cancer on imaging tests, continued use of levothyroxine to keep the TSH level low is recommended. Surveillance with Tg testing and ultrasound will continue. Other imaging procedures such as CT or MRI are ordered as needed.

If the Tg level begins to rise steadily but imaging tests (including a PET scan) do not find cancer, RAI therapy may be an option. If the therapy is effective, additional RAI treatments may be considered. There should be a minimum of 6 to 12 months between RAI treatments.

Cancer that returns to the neck

If the cancer returns to the neck, surgery, RAI therapy, or both may be used to treat it. If the cancer can be removed based on its size and location, surgery is preferred.

In some cases, monitoring the cancer closely instead of treating it may be an option. If the cancer isn't getting worse and isn't close to any critical structures, a watch-and-wait approach may be appropriate.

If the cancer cannot be removed with surgery, does not take up iodine, and is getting worse (progressing), treatment with radiation therapy,

targeted therapy, or both may be an option. Recommended targeted therapies for cancer that cannot be removed with surgery and is progressing are listed in [Guide 1](#).

If the therapies listed in [Guide 1](#) are not available, your treatment team may recommend others not listed here. In this case, joining a clinical trial is strongly encouraged.

Metastatic cancer

Thyroid cancer that spreads to areas far from the neck is known as metastatic. The distant areas of cancer are called metastases. Metastases can form in the lungs, liver, muscles, bones, brain, and spinal cord.

If the cancer takes up iodine, RAI therapy is recommended to treat metastatic papillary, follicular, or Hürthle cell thyroid cancers. Local therapies may also be used to treat areas of cancer directly.

If RAI therapy isn't an option

If the cancer doesn't take up iodine, treatment options include:

- Targeted therapy

Guide 1

Targeted therapy for papillary, follicular, and Hürthle cell cancers

For worsening and/or symptomatic cancer	<ul style="list-style-type: none"> • Lenvatinib (Lenvima[®]) (preferred) • Sorafenib (Nexavar[®])
For <i>NTRK</i> gene mutations	<ul style="list-style-type: none"> • Larotrectinib (Vitrakvi[®]) • Entrectinib (Rozlytrek[®])
For <i>RET</i> gene mutations	<ul style="list-style-type: none"> • Selpercatinib (Retevmo[®])
For tumors with a high number of mutations	<ul style="list-style-type: none"> • Pembrolizumab (Keytruda[®])

- Treating the metastases directly
- Joining a clinical trial
- Best supportive care

These options are described in more detail next. You will continue to take levothyroxine to keep your TSH level down.

Targeted therapy

If RAI therapy is not possible, targeted therapy may be an option. However, if the metastases are not growing (or growing very slowly) and not causing symptoms, monitoring the cancer may be a better option.

In order to select the targeted therapy with the best chance of working, testing to identify *NTRK* and *RET* gene mutations and to determine the total number of mutations (tumor mutational burden) is recommended.

Recommended targeted therapies for metastatic cancer that cannot be treated with surgery or RAI are listed in [Guide 1](#).

Other systemic therapies are available and may be recommended if those listed in [Guide 1](#) are not available or appropriate. Joining a clinical trial is strongly encouraged for everyone with metastatic thyroid cancer.

Local therapies

Small tumors can be treated directly using one or more types of local therapy.

If the cancer has only spread to a limited number of sites, or has spread to bone and/or is causing symptoms, it may be possible to remove or destroy the metastases with surgery and/or radiation therapy. Ablation is another method used to treat small bone

tumors. In ethanol ablation, a concentrated alcohol solution is injected into the neck to kill cancer cells. Cryoablation involves applying an extremely cold “wand” directly into the tumor. Radiofrequency ablation uses radiofrequency waves that generate heat to kill cancer cells. Stereotactic body radiotherapy (SBRT) is a special ablative radiation technique that uses high doses of radiation to small areas to kill cancer cells.

Your doctor may recommend intravenous bisphosphonate or denosumab. These are bone-strengthening medications that can slow damage caused by bone metastases and help relieve symptoms.

If the cancer has spread to the brain or spinal cord (the central nervous system), options for treatment may include surgery to remove the metastases. Stereotactic radiosurgery is a non-surgical and highly precise type of radiation therapy that can be used to treat small brain tumors.

Clinical trial

Joining a clinical trial is strongly encouraged for everyone with metastatic thyroid cancer. Ask your treatment team if there is an open clinical trial you might be eligible for. See page 17 and the last chapter of this book for more information.

Best supportive care

Supportive care plays an essential role in the care of people with metastatic thyroid cancer. In addition to providing relief from symptoms caused by cancer and its treatment, supportive care can provide emotional, spiritual, and social support.

Review

- Papillary, follicular, and Hürthle cell are differentiated thyroid cancers. This means the cancer cells look similar to normal cells under a microscope.
- Differentiated cancers tend to grow and spread slowly. They usually have good treatment outcomes.
- Total thyroidectomy is an option for all of the differentiated cancers. Lobectomy may also be an option for small, low-risk cancers.
- Total thyroidectomy is recommended for any cancer that has grown or spread beyond the thyroid.
- RAI therapy will be considered if the results of surgery are very good.
- After a total thyroidectomy, lifelong thyroid hormone replacement therapy is needed. Levothyroxine is almost always used.
- Hormone replacement therapy is not always needed after lobectomy, because the remaining lobe of the thyroid is still making hormones.

3

Medullary thyroid cancer

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34 If cancer returns or spreads

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The most common types of thyroid cancer start in follicular cells, where thyroid hormone is made. Medullary thyroid cancer starts in C cells, which make a different hormone called calcitonin. Medullary thyroid cancer behaves somewhat differently than the differentiated thyroid cancers.

About 1 in 4 medullary thyroid cancers is caused by a mutation of the *RET* gene. *RET* mutations can be passed from parent to child (inherited). The hereditary form of medullary thyroid cancer is known as multiple endocrine neoplasia type 2 (MEN2).

Compared to non-inherited (“sporadic”) medullary thyroid cancer, the hereditary form tends to start at a much younger age and behave more aggressively. For this reason, the thyroid is removed at a very young age in infants and children known to have a *RET* mutation.

Inherited medullary thyroid cancer also tends to spread to lymph nodes or distant parts of the body earlier and more often than non-hereditary medullary thyroid cancer. The cancer can spread to the lungs, liver, or bones.

There are many different possible mutations of the *RET* gene. Some are more likely to cause thyroid cancer than others. Some are also associated with more aggressive thyroid cancer.

The specific *RET* mutation can affect:

- The overall chance of developing thyroid cancer

- When thyroid cancer starts
- How aggressive/fast-growing the thyroid cancer will be

MEN2A, also known as familial medullary thyroid carcinoma (FMTC), is generally considered moderate risk. In people with MEN2A the parathyroid glands can make too many hormones (hyperparathyroidism) and may need to be removed. MEN2B is caused by higher-risk mutations of the *RET* gene.

Testing

If a needle biopsy (FNA) diagnoses medullary thyroid cancer, more testing will be ordered. Genetic testing and counseling, blood and laboratory tests, and imaging procedures are used to help plan the best treatment.

Genetic testing and counseling

Everyone with medullary thyroid cancer found by FNA should be tested for mutations of the *RET* gene. Those who have a *RET* mutation will be referred to a genetic counselor. This specially trained health professional can explain the test results and provide information, counseling, and support. The counselor can explain what the results mean for members of your family, and who should also seek testing for the same mutation.

Blood tests

Before treatment, blood tests will be ordered to measure the levels of calcitonin, calcium, and carcinoembryonic antigen (CEA). CEA is a protein that can be found in the blood of people with medullary thyroid cancer and some other cancers. It may also be used to check treatment results and monitor for the return of cancer.

Pheochromocytoma testing

A pheochromocytoma is a usually benign tumor that forms in the adrenal gland (gland located above the kidney). It causes the adrenal gland to make too much adrenaline (“fight-or-flight”) hormone. Pheochromocytomas can cause symptoms such as high blood pressure, headaches, heart palpitations, flushing of the face, nausea, and vomiting. While most are not cancer, it is important to have a blood test for pheochromocytomas before surgery. They can increase the risk of serious cardiac issues during surgery.

Imaging procedures

If an ultrasound of the thyroid and neck has not yet been done, it is recommended before surgery. Some people will also have an examination of the voice box and vocal cords. This is called laryngoscopy. A vocal cord exam may be helpful in patients with voice changes, invasive cancer, or large (bulky) cancer in the middle of the neck. It may also be ordered in those who have had surgery involving nerves near the voice box.

Other imaging procedures are generally ordered on an as-needed basis. These may include computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET), bone scan, and skeletal MRI.

Staging

The results of the testing described above are used to determine the spread of cancer in the body, also known as the cancer stage.

In the early stages of medullary thyroid cancer, the tumor has not spread beyond the thyroid. A 2 cm or smaller tumor (about the size of a peanut) is stage 1. A tumor between 2 and 4 cm is stage 2. In stage 3, cancer has spread to nearby lymph nodes. The tumor itself may be small or large.

There are three categories of stage 4 medullary cancer. Stage 4A is moderately advanced disease. The tumor has grown extensively into the neck, or has spread to lymph nodes far from the thyroid.

Stage 4B is considered very advanced disease. Although there is no cancer in nearby lymph nodes, the tumor has invaded critical areas or structures such as the spine, large blood vessels, or the carotid artery.

Stage 4C is the most advanced stage, metastatic. The cancer has spread to areas of the body far from the thyroid.

Treatment

Sporadic (non-inherited) medullary thyroid cancer

Medullary thyroid cancer is treated with surgery to remove the entire thyroid (total thyroidectomy). Depending on the size and location of the tumor, the surgeon may also remove nearby lymph nodes that are known or suspected to have cancer. This is known as neck dissection. Neck dissection may not be needed for some tumors smaller than 1 centimeter (about the size of a pea).

Levothyroxine is given after surgery to replace the hormones no longer being supplied by the thyroid. Hormone replacement therapy is generally needed lifelong after a thyroidectomy.

See the following page for information on what to expect after surgery.

Hereditary medullary thyroid cancer

Treatment of both forms of hereditary medullary thyroid cancer is similar.

MEN2A

MEN2A or familial thyroid cancer is treated using total thyroidectomy. In infants or young children known to have this type of inherited medullary thyroid cancer, it is recommended that the thyroid be removed before age 5.

Lymph nodes near the thyroid may also be removed during surgery. Reasons for removing lymph nodes may include high calcitonin or CEA levels before surgery, or abnormal ultrasound results.

If the parathyroid glands are making too much parathyroid hormone, one or more of the glands

may be removed during surgery. Some or all of the tissue of individual parathyroid glands may be removed.

Parathyroid tissue can be removed and transplanted into another area of the body, such as the forearm. Over time, the parathyroid tissue begins to make hormones again. Parathyroid gland tissue can also be frozen and stored outside the body (cryopreservation). This preserves the tissue so that it can be put back in the body at a later date.

Levothyroxine is given after surgery to replace the hormones no longer being supplied by the thyroid. Hormone replacement therapy is generally needed lifelong after a thyroidectomy.

See the following page for information on what to expect after surgery.

MEN2B

Like MEN2A, MEN2B is treated using total thyroidectomy. In infants known to have this type of inherited medullary thyroid cancer, it is recommended that the thyroid be removed by age 1.

In addition to the thyroid gland, any neck lymph nodes known or suspected to have cancer will be removed. Lymph nodes without cancer may also be removed in order to prevent any cancer cells from spreading to them.

Levothyroxine is given after surgery to replace the hormones no longer being supplied by the thyroid. Hormone replacement therapy is generally needed lifelong after a thyroidectomy.

See the following page for information on what to expect after surgery.



Thyroidectomy should be performed by a surgeon and team experienced in performing pediatric thyroid surgery.

After surgery

After a thyroidectomy, the best way to monitor for the return of medullary thyroid cancer is to check the levels of calcitonin and CEA on a regular basis. The calcitonin level after surgery is particularly important. The lower the calcitonin level, the better.

The first blood test will take place 2 to 3 months after surgery. It is important to wait a few months before testing because it takes time for the calcitonin level to drop after the thyroid is removed.

Normal blood test results

If the first blood test after surgery does not detect calcitonin and CEA is within normal range, the cancer is likely cured. Going forward, the calcitonin and CEA levels should be measured every year. If either level begins to rise, further testing and workup is needed.

Additional testing for inherited MTC

In addition to annual calcitonin and CEA testing, yearly testing for pheochromocytoma is recommended for people with an inherited medullary thyroid cancer (MEN2A or MEN2B). In those with MEN2A, yearly testing for hyperparathyroidism is also recommended.

Abnormal blood test results

If the first blood test after surgery finds calcitonin, or if the level of CEA is high, the cancer may not have been completely removed during surgery. Or, the cancer may have returned or spread.

Imaging tests of the neck, liver, chest, and/or bones may be ordered to look for cancer. If the imaging procedures find cancer, or if you are having symptoms, see the next section, *If cancer returns or spreads*.

If the imaging tests do not find anything concerning and you are not having symptoms, you will be closely monitored. Blood tests to measure calcitonin and CEA are recommended every 6 to 12 months. Depending on how quickly the levels are rising, imaging procedures or more frequent testing may be needed. In some cases, another surgery may be considered to remove remaining cancer.

If cancer returns or spreads

Cancer that returns to the neck

Surgery is the preferred treatment for medullary thyroid cancer that returns to the neck area. If surgery is not possible, radiation therapy may be used instead. Taking a watch-and-wait approach by monitoring the cancer can also be an appropriate option for some recurrent medullary thyroid cancers.

If the cancer cannot be removed using surgery and is causing symptoms or getting worse (progressing), targeted therapy is often a treatment option. Currently preferred targeted therapies include:

- Vandetanib (Caprelsa®)
- Cabozantinib (Cabometyx®)
- Selpercatinib (Retevmo®) (for *RET* mutation-positive cancers)

In some cases, the targeted therapy pembrolizumab (Keytruda®) may be useful. It may be given when testing shows a high number of mutations.

Metastatic cancer

Treatment of metastatic medullary thyroid cancer depends in part on whether the cancer is causing symptoms. If the cancer is stable and is not causing symptoms, treatment is not always needed. Surgery, ablation, or other techniques to remove or destroy the metastases may be considered.

If the cancer progresses (gets worse) and begins causing symptoms, systemic therapy is often a treatment option. The same targeted therapies described above are preferred for

metastatic disease. If the preferred therapies are not available or effective, other “small-molecule” kinase inhibitors may be considered. Chemotherapy that includes the drug dacarbazine (“DTIC”) may also be an option.

Radiation therapy may be used to help with symptoms, or as an ablative treatment in some cases. Surgery, ablation, or other techniques may be used to treat metastases in order to relieve symptoms.

If the cancer has spread to bone, intravenous bisphosphonates or denosumab are recommended. These are bone-strengthening medications that can slow damage caused by bone metastases and help relieve symptoms.

Clinical trial

Joining a clinical trial is strongly encouraged for everyone with metastatic thyroid cancer. Ask your treatment team if there is an open clinical trial you might be eligible for. See page 17 and the last chapter of this book for more information.

Best supportive care

Supportive care plays an essential role in the care of people with metastatic thyroid cancer. In addition to providing relief from symptoms caused by cancer and its treatment, supportive care can provide emotional, spiritual, and social support.

Review

- ▶ Medullary thyroid cancer starts in the C cells of the thyroid. The C cells make a hormone called calcitonin.
- ▶ About 1 out of 4 medullary thyroid cancers is inherited.
- ▶ Inherited medullary thyroid cancer is caused by mutations of the *RET* gene.
- ▶ Any person diagnosed with medullary thyroid cancer using FNA (needle biopsy) should be tested for *RET* mutations and receive genetic counseling.
- ▶ Inherited medullary thyroid cancer is known as multiple endocrine neoplasia type 2 (MEN2).
- ▶ All medullary thyroid cancers are treated with total thyroidectomy.
- ▶ Blood tests to measure CEA and calcitonin are recommended to monitor for the return of medullary thyroid cancer.
- ▶ Surgery is the preferred treatment for cancer that returns to the neck. Other options may include radiation therapy, monitoring (no treatment), and targeted therapy.
- ▶ Surgery, radiation therapy, or other techniques may be used to remove or destroy metastases and relieve symptoms.
- ▶ Supportive care can help relieve symptoms caused by medullary thyroid cancer and its treatment.

4

Anaplastic thyroid cancer

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- 37 Treatment options
- 39 Important conversations
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- 40 Review



Anaplastic is the least common and most aggressive type of thyroid cancer. About half of people with this type have (or had) a more common type of thyroid cancer. Anaplastic thyroid cancer generally can't be cured. Supportive care is essential throughout the treatment process.

Testing and staging

If a needle biopsy diagnoses anaplastic thyroid cancer, more testing is needed to confirm the diagnosis and learn the extent of the cancer. Testing typically includes:

- ▶ Blood tests, including thyroid-stimulating hormone (TSH)
- ▶ Imaging procedures to see inside the head, neck, chest, abdomen, pelvis, voice box (larynx), and airway (trachea)
- ▶ Genetic testing for mutations of *BRAF*, *NTRK*, *ALK*, and *RET* genes and for total number of mutations

The results of testing are used to determine the spread of cancer in the body, also known as the cancer stage.

All anaplastic thyroid cancers are stage 4. The letters A, B, and C are used to describe how far the cancer has spread at the time it is found. Stages 4A and 4B are nonmetastatic. The cancer is either only in the thyroid (stage 4A) or may have spread to nearby lymph nodes (4B). Stage 4C is metastatic disease. The cancer has spread to areas of the body far from the thyroid.

Treatment options

Treatment options for anaplastic thyroid cancer depend in part on whether the cancer has spread to areas far from the thyroid (metastasized).

Nonmetastatic cancer

Treatment of nonmetastatic anaplastic thyroid cancer (stages 4A and 4B) depends on whether the tumor can safely be removed using surgery. If surgery is an option, the entire thyroid is removed (total thyroidectomy). Nearby lymph nodes known or suspected to have cancer are also removed.

If surgery successfully removes all of the cancer, or if only tiny amounts remain, radiation therapy to kill leftover cancer cells is next. Sometimes radiation therapy is used in combination with chemotherapy. When given with radiation, some chemotherapy medicines make it easier for radiation to kill cancer cells. This is called radiosensitizing chemotherapy. Not everyone will undergo chemotherapy in addition to radiation therapy.

If surgery is not an option

If the cancer cannot safely be removed using surgery, radiation therapy is used instead. Chemotherapy may be given in addition to radiation therapy. After radiation therapy (and chemotherapy, if received), surgery may be an option. This will depend on the size of the tumor after radiation and other factors.

Metastatic cancer

If anaplastic thyroid cancer spreads to distant areas of the body, there may be more than one approach to treatment. Some people choose to treat the cancer aggressively. Others choose to

maximize their quality of life. Talk to your care team about the approach that aligns with your health and personal preferences.

Option: Aggressive treatment

If you and your treatment team decide on this option, all of the following treatments may be used together to fight the cancer:

- Total thyroidectomy and lymph node dissection
- Radiation therapy
- Targeted therapy or chemotherapy (see [Guide 2](#))

Joining a clinical trial may be another option. Participation in clinical trials is strongly encouraged for all patients with metastatic anaplastic thyroid cancer. Ask your treatment team if there are any open trials that you

may be eligible for. See page 17 for more information.

Option: Maximize quality of life

Aggressive treatment is not an option for everyone with metastatic anaplastic thyroid cancer. It may not be recommended for health reasons, or it may not align with your preferences. Everyone's cancer—and priorities—are different. For some, living as comfortably as possible for as long as possible is preferred to undergoing harsh treatments.

In this approach, the thyroid is not removed. Surgery, radiation therapy, or both are used to control cancer growth throughout the body. Removing or destroying areas of cancer directly can help relieve symptoms caused by cancer in the neck or distant areas.

If anaplastic thyroid cancer has spread to bones, denosumab (Prolia[®]) or medications

Guide 2

Systemic therapy for metastatic anaplastic thyroid cancer

Preferred options

- Dabrafenib/trametinib (*BRAF* V600E mutation positive)
- Larotrectinib (*NTRK* gene fusion positive)
- Entrectinib (*NTRK* gene fusion positive)
- Selpercatinib (*RET* fusion positive)

Other recommended options

- Paclitaxel/carboplatin
- Docetaxel/doxorubicin
- Paclitaxel
- Doxorubicin

Useful in some circumstances

- Lenvatinib (Lenvima[®]) (if cure is not possible and other therapies are not an option)
- Pembrolizumab (Keytruda[®]) (if the total number of mutations is high)

called bisphosphonates may be given to help strengthen bones, slow bone damage, and relieve symptoms caused by the tumors.

Supportive care plays an essential role in the care of patients with anaplastic thyroid cancer.

Important conversations

Important, often difficult, discussions are needed after a diagnosis of anaplastic thyroid cancer. These discussions can help with making decisions about treatment and other care.

Prognosis

Prognosis refers to the expected outcome or course of an individual cancer. The prognosis for most anaplastic thyroid cancers is poor, meaning that good outcomes are unlikely. Discussing prognosis is an important part of care planning for anaplastic thyroid cancer. Your prognosis can affect the type and number of treatments that you may be willing, or able, to receive.

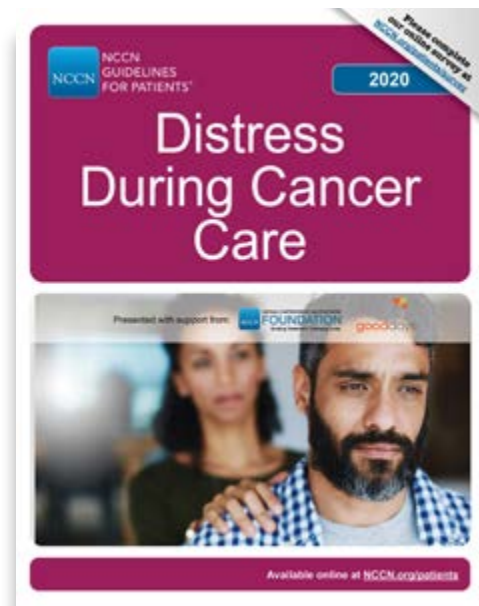
Weigh treatment options

Consider and discuss the goals of treatment with your care team. Care to improve quality of life may be more helpful than cancer treatment. Talk to your doctor about your treatment options. For example, controlling the tumor growth may be preferred to aggressive treatment. Participation in clinical trials is strongly recommended for all patients with anaplastic thyroid cancer. Talk to your treatment team about clinical trials you may be eligible for.

Palliative care

Supportive care is available for everyone with anaplastic thyroid cancer. Supportive care can provide relief from symptoms as well as emotional, social, and spiritual support. Your doctor may suggest hospice care during this time.

Hospice care can help with the physical and emotional needs of anaplastic thyroid cancer. See *NCCN Guidelines for Patients: Distress During Cancer Care* available at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines):



Monitoring and management

Imaging procedures (CT or MRI) of the brain, neck, chest, abdomen, and pelvis are needed on a regular basis for metastatic anaplastic thyroid cancer. There is not a one-size-fits-all schedule for these scans. Talk to your treatment team about how often imaging procedures are needed. A combined PET/CT scan may be ordered 3 to 6 months after treatment of metastatic disease to determine the extent of the cancer.

If surveillance testing continues to find no evidence of disease (NED), monitoring will continue. Surgery, radiation therapy, or both are used to control cancer growth throughout the body. If the cancer returns or gets worse (progresses), trying a different systemic therapy may be an option. Joining a clinical trial is strongly encouraged if one is available to you.

Review

- Anaplastic is the least common and most aggressive type of thyroid cancer.
- Supportive care is available and is essential for everyone with anaplastic thyroid cancer.
- Supportive care can help relieve the physical side effects of cancer and its treatment. It can also provide mental, social, and spiritual care and support.
- All anaplastic thyroid cancers are stage 4. The letters A, B, and C are used to describe how far the cancer has spread at the time it is found.
- If surgery is possible, nonmetastatic anaplastic thyroid cancer is treated with total thyroidectomy and lymph node dissection.
- Radiation therapy—sometimes in combination with chemotherapy—is used to kill cancer cells remaining after surgery.
- If surgery is not an option for nonmetastatic anaplastic thyroid cancer, radiation therapy is typically used instead. Radiation therapy may be given in combination with chemotherapy.
- Treatment of metastatic anaplastic thyroid cancer (stage 4C) may focus on maximizing quality of life rather than treating the cancer.
- Aggressive therapy for metastatic cancer includes total thyroidectomy, radiation therapy, and systemic therapy.

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Survivorship

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Survivorship focuses on the physical, emotional, and financial issues unique to cancer survivors. Managing the long-term side effects of cancer, staying connected with your primary care doctor, and living a healthy lifestyle are important parts of survivorship.

Thyroid cancer survivors may experience long-term health effects of cancer and its treatment. Such side effects can may include:

- Osteoporosis
- High blood pressure
- Heart rhythm disorders
- Heart valve disease

These conditions depend in part on the thyroid cancer treatments used. Surgery, radiation therapy, RAI therapy, and hormone replacement therapy all have unique potential side effects.

Staying connected with your primary care doctor and adopting healthy habits can help prevent or offset long-term side effects of cancer treatment. It can also help lower the risk of getting other types of cancer.

Your primary care doctor

After finishing cancer treatment, your primary care doctor will play an important role in your care. Your cancer doctor and primary doctor should work together to make sure you get the follow-up care you need. Your oncologist should develop a survivorship care plan that includes:

- A summary of all cancer-related treatment(s) you've had (surgeries, chemotherapy, radiation, etc.)
- A description of the possible late- and long-term side effects
- Recommendations for monitoring for the return of cancer
- Information on when your care will be transferred to your primary care physician (PCP). The plan should also outline specific responsibilities for both your cancer doctor and your PCP.
- Recommendations on your overall health and well-being.

Healthy habits

Monitoring for the return of cancer is important after finishing treatment. But it is also important to keep up with other aspects of your health. Steps you can take to help prevent other health issues and to improve your quality of life are described next.

Get screened for other types of cancer. Your primary care doctor should tell you what cancer screening tests you should have based on your gender, age, and risk level.

Get other recommended health care for your age and gender, such as blood pressure screening, hepatitis C screening, and immunizations (such as the flu shot).

Maintain a healthy body weight. Try to exercise at a moderate intensity for at least 30 minutes most days of the week. Eat a healthy diet with

lots of plant-based foods, including vegetables, fruits, and whole grains.

Drink little to no alcohol. This means no more than 1 drink/day for women, and no more than 2 drinks/day for men.

If you are a smoker, quit! Your doctor will be able to provide (or refer you for) counseling on how to stop smoking.

Healthy eating

Experts recommend eating a healthy diet, especially one that includes a lot of plant-based foods (veggies, fruits, and whole grains).



Reduce alcohol

Cutting back on alcohol is an important part of staying healthy. Experts recommend no more than 1 drink per day for women, and no more than 2 drinks per day for men.



Review

- Survivorship focuses on the physical, emotional, and financial issues unique to cancer survivors.
- Your oncologist and primary care doctor should work together to make sure you get the follow-up care you need.
- A survivorship care plan is helpful in transitioning your care to your primary care doctor.
- Healthy habits, including exercising and eating right, play an important role in helping to prevent other diseases and second cancers.

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Making treatment decisions

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It's important to be comfortable with the cancer treatment you choose. This choice starts with having an open and honest conversation with your doctor.

It's your choice

In shared decision-making, you and your doctors share information, discuss the options, and agree on a treatment plan. It starts with an open and honest conversation between you and your doctor.

Treatment decisions are very personal. What is important to you may not be important to someone else.

Some things that may play a role in your decision-making:

- What you want and how that might differ from what others want
- Your religious and spiritual beliefs
- Your feelings about certain treatments like surgery or chemotherapy
- Your feelings about pain or side effects such as nausea and vomiting
- Cost of treatment, travel to treatment centers, and time away from work
- Quality of life and length of life
- How active you are and the activities that are important to you

Think about what you want from treatment. Discuss openly the risks and benefits of specific treatments and procedures. Weigh options and share concerns with your doctor. If you take the

time to build a relationship with your doctor, it will help you feel supported when considering options and making treatment decisions.

Second opinion

It is normal to want to start treatment as soon as possible. While cancer can't be ignored, there is time to have another doctor review your test results and suggest a treatment plan. This is called getting a second opinion, and it's a normal part of cancer care. Even doctors get second opinions!

Things you can do to prepare:

- Check with your insurance company about its rules on second opinions. There may be out-of-pocket costs to see doctors who are not part of your insurance plan.
- Make plans to have copies of all your records sent to the doctor you will see for your second opinion.

Support groups

Many people diagnosed with cancer find support groups to be helpful. Support groups often include people at different stages of treatment. Some people may be newly diagnosed, while others may be finished with treatment. If your hospital or community doesn't have support groups for people with cancer, check out the websites listed in this book.

Questions to ask your doctors

Possible questions to ask your doctors are listed on the following pages. Feel free to use these questions or come up with your own. Be clear about your goals for treatment and find out what to expect from treatment.

Websites

American Thyroid Association (ATA)

thyroid.org/patient-thyroid-information

Head and Neck Cancer Alliance

headandneck.org

Support for People with Oral and Head and Neck Cancer (SPOHNC)

spohnc.org

The THANC Foundation

thancfoundation.org

Thyroid Care Collaborative

thyroidccc.org

ThyCa: Thyroid Cancer Survivors' Association, Inc.

thyca.org

U.S. National Library of Medicine Clinical Trials Database

clinicaltrials.gov



Words to know

anaplastic thyroid cancer

A rare and aggressive type of thyroid cancer. Anaplastic cells look very different from normal thyroid cells.

biopsy

Removal of small amounts of tissue or fluid to be tested for disease.

C cells

Cells in the thyroid that make calcitonin. These cells are also called parafollicular cells.

calcitonin

A hormone made by the C cells of the thyroid gland. It helps control the calcium level in the blood.

central nervous system

The brain and spinal cord.

chemotherapy

Drugs that work throughout the body to kill cancer cells.

clinical trial

Research on a test or treatment to assess its safety or how well it works.

computed tomography (CT)

A test that uses x-rays to view body parts.

contrast

A substance put into your body to make clearer pictures during imaging tests.

deoxyribonucleic acid (DNA)

A chain of chemicals inside cells that contains coded instructions for making and controlling cells.

hormone

One of many substances made by glands in the body. Some hormones can also be made

in the laboratory. Hormones circulate in the bloodstream and control the actions of certain cells or organs.

magnetic resonance imaging (MRI)

A test that uses radio waves and powerful magnets to make pictures of the insides of the body.

medullary thyroid cancer

A type of thyroid cancer that starts in the C cells that make calcitonin.

metastasis

The spread of cancer cells from the first tumor to another body part.

molecular test

A test of abnormal coded instructions in cells or the proteins that help cancer cells grow.

multidisciplinary team

A group of health care professionals who are experts in different areas of treatment related to cancer.

neck dissection

Removal of the lymph nodes and other tissue in the neck area.

nodule

A small mass of abnormal tissue.

observation

A period of scheduled follow-up testing to watch for signs of cancer spread (metastasis) or return (recurrence).

papillary thyroid cancer

The most common type of thyroid cancer. Starts in follicular cells.

parathyroid gland

One of four small glands near the thyroid that make parathyroid hormone.

pathologist

An expert in examining cells to find disease.

pathology report

A document with information about cells and tissue removed from the body and examined with a microscope for disease.

pituitary gland

A gland found near the base of the brain. It makes hormones that control how other glands in the body work or make hormones.

positron emission tomography (PET)

A test that uses radioactive material to see the shape and function of body parts.

prognosis

The expected pattern and outcome of a disease.

supportive care

Care given to improve the quality of life of patients who have a serious or life-threatening disease. Also called palliative care.

thyroid

A gland located beneath the larynx (voice box) that makes thyroid hormone and calcitonin. The thyroid gland helps regulate growth and metabolism.

Thyrogen

A form of thyroid-stimulating hormone (TSH) made in the laboratory. It is used to test for remaining or recurring cancer cells in patients who have been treated for thyroid cancer. Also called thyrotropin alfa.

thyroxine

A hormone made by the thyroid gland and contains iodine. Also called T4.

triiodothyronine

A thyroid hormone. Also called T3.

tumor

An abnormal mass of cells.

tumor mutational burden (TMB)

The total number of mutations (changes) found in the DNA of cancer cells.

ultrasound

A test that uses sound waves to take pictures of the inside of the body.

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For disclosures, visit [NCCN.org/about/disclosure.aspx](https://www.nccn.org/about/disclosure.aspx).

NCCN Cancer Centers

Abramson Cancer Center
at the University of Pennsylvania
Philadelphia, Pennsylvania
800.789.7366 • penncancer.org

Fred & Pamela Buffett Cancer Center
Omaha, Nebraska
402.559.5600 • unmc.edu/cancercenter

Case Comprehensive Cancer Center/
University Hospitals Seidman Cancer
Center and Cleveland Clinic Taussig
Cancer Institute
Cleveland, Ohio
800.641.2422 • UH Seidman Cancer Center
uhhospitals.org/services/cancer-services
866.223.8100 • CC Taussig Cancer Institute
my.clevelandclinic.org/departments/cancer
216.844.8797 • Case CCC
case.edu/cancer

City of Hope National Medical Center
Los Angeles, California
800.826.4673 • cityofhope.org

Dana-Farber/Brigham and
Women's Cancer Center
Boston, Massachusetts
617.732.5500
youhaveus.org

Massachusetts General Hospital
Cancer Center
Boston, Massachusetts
617.726.5130
massgeneral.org/cancer-center

Duke Cancer Institute
Durham, North Carolina
888.275.3853 • dukecancerinstitute.org

Fox Chase Cancer Center
Philadelphia, Pennsylvania
888.369.2427 • foxchase.org

Huntsman Cancer Institute
at the University of Utah
Salt Lake City, Utah
800.824.2073
huntsmancancer.org

Fred Hutchinson Cancer
Research Center/Seattle
Cancer Care Alliance
Seattle, Washington
206.606.7222 • seattlecca.org
206.667.5000 • fredhutch.org

The Sidney Kimmel Comprehensive
Cancer Center at Johns Hopkins
Baltimore, Maryland
410.955.8964
www.hopkinskimmellcancercenter.org

Robert H. Lurie Comprehensive
Cancer Center of Northwestern
University
Chicago, Illinois
866.587.4322 • cancer.northwestern.edu

Mayo Clinic Cancer Center
Phoenix/Scottsdale, Arizona
Jacksonville, Florida
Rochester, Minnesota
480.301.8000 • Arizona
904.953.0853 • Florida
507.538.3270 • Minnesota
mayoclinic.org/cancercenter

Memorial Sloan Kettering
Cancer Center
New York, New York
800.525.2225 • mskcc.org

Moffitt Cancer Center
Tampa, Florida
888.663.3488 • moffitt.org

The Ohio State University
Comprehensive Cancer Center -
James Cancer Hospital and
Solove Research Institute
Columbus, Ohio
800.293.5066 • cancer.osu.edu

O'Neal Comprehensive
Cancer Center at UAB
Birmingham, Alabama
800.822.0933 • uab.edu/onealcancercenter

Roswell Park Comprehensive
Cancer Center
Buffalo, New York
877.275.7724 • roswellpark.org

Siteman Cancer Center at Barnes-
Jewish Hospital and Washington
University School of Medicine
St. Louis, Missouri
800.600.3606 • siteman.wustl.edu

St. Jude Children's Research Hospital
The University of Tennessee
Health Science Center
Memphis, Tennessee
866.278.5833 • stjude.org
901.448.5500 • uthsc.edu

Stanford Cancer Institute
Stanford, California
877.668.7535 • cancer.stanford.edu

UC San Diego Moores Cancer Center
La Jolla, California
858.822.6100 • cancer.ucsd.edu

UCLA Jonsson
Comprehensive Cancer Center
Los Angeles, California
310.825.5268 • cancer.ucla.edu

UCSF Helen Diller Family
Comprehensive Cancer Center
San Francisco, California
800.689.8273 • cancer.ucsf.edu

University of Colorado Cancer Center
Aurora, Colorado
720.848.0300 • coloradocancercenter.org

University of Michigan
Rogel Cancer Center
Ann Arbor, Michigan
800.865.1125 • rogelcancercenter.org

The University of Texas
MD Anderson Cancer Center
Houston, Texas
844.269.5922 • mdanderson.org

University of Wisconsin
Carbone Cancer Center
Madison, Wisconsin
608.265.1700 • uwhealth.org/cancer

UT Southwestern Simmons
Comprehensive Cancer Center
Dallas, Texas
214.648.3111 • utsouthwestern.edu/simmons

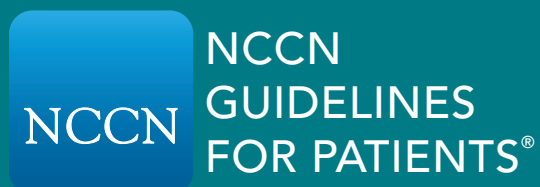
Vanderbilt-Ingram Cancer Center
Nashville, Tennessee
877.936.8422 • vicc.org

Yale Cancer Center/
Smilow Cancer Hospital
New Haven, Connecticut
855.4.SMILOW • yalecancercenter.org

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Thyroid Cancer

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