(Papillary and Follicular)

WHAT IS THE THYROID GLAND?

The thyroid gland is a butterfly-shaped endocrine gland that is normally located in the lower front of the neck. The thyroid's job is to make thyroid hormones, which are secreted into the blood and then carried to every tissue in the body. Thyroid hormone helps the body use energy, stay warm and keep the brain, heart, muscles, and other organs working as they should.

CANCER OF THE THYROID

Thyroid cancer is relatively uncommon compared to other cancers. In the United States it is estimated that in 2016 approximately 64,000 new patients will be diagnosed with thyroid cancer, compared to over 240,000 patients with breast cancer and 135,000 patients with colon cancer. However, fewer than 2000 patients die of thyroid cancer each year. In 2013, the last year for which statistics are available, over 630,000 patients were living with thyroid cancer in the United States. Thyroid cancer is usually very treatable and is often cured with surgery (see Thyroid Surgery brochure) and, if indicated, radioactive iodine (see Radioactive Iodine brochure). Even when thyroid cancer is more advanced, effective treatment is available for the most common forms of thyroid cancer. Even though the diagnosis of cancer is terrifying, the prognosis for most patients with papillary and follicular thyroid cancer is usually excellent.

WHAT ARE THE TYPES OF THYROID CANCER?

Papillary thyroid cancer. Papillary thyroid cancer is the most common type, making up about 70% to 80% of all thyroid cancers. Papillary thyroid cancer can occur at any age. It tends to grow slowly and often spreads to lymph nodes in the neck. However, unlike many other cancers, papillary cancer has a generally excellent outlook, even if there is spread to the lymph nodes.

Follicular thyroid cancer. Follicular thyroid cancer makes up about 10% to 15% of all thyroid cancers in the United States. Follicular cancer can spread to lymph nodes in the neck, but this is much less common than with papillary cancer. Follicular cancer is also more likely than papillary cancer to spread to distant organs, particularly the lungs and bones.

Papillary and follicular thyroid cancers are also known as Well-Differentiated Thyroid Cancers (DTC). The information in this brochure refers to the differentiated thyroid cancers. The other types of thyroid cancer listed below will be covered in other brochures

Medullary thyroid cancer. Medullary thyroid cancer (MTC), accounts for approximately 2% of all thyroid cancers. Approximately 25% of all MTC runs in families and is associated with other endocrine tumors (see *Medullary Thyroid Cancer brochure*). In family members of an affected person, a test for a genetic mutation in the RET proto-oncogene can lead to an early diagnosis of medullary thyroid cancer and, as a result, to curative surgery.

Anaplastic thyroid cancer. Anaplastic thyroid cancer is the most advanced and aggressive thyroid cancer and the least likely to respond to treatment. Anaplastic thyroid cancer is very rare and is found in less than 2% of patients with thyroid cancer. (See *Anaplastic thyroid cancer brochure*.)

WHAT ARE THE SYMPTOMS OF THYROID CANCER?

Thyroid cancer often presents as a lump or nodule in the thyroid and usually does not cause any symptoms (see *Thyroid Nodule brochure*). Blood tests generally do not help to find thyroid cancer and thyroid blood tests such as TSH are usually normal, even when a cancer is present. Neck examination by your doctor is a common way in which thyroid nodules and thyroid cancer are found. Often, thyroid nodules are discovered incidentally on imaging tests like CT scans and neck ultrasound done for completely unrelated reasons. Occasionally, patients themselves find thyroid nodules by noticing a lump in their neck while looking in a mirror, buttoning their collar, or fastening a necklace. Rarely, thyroid cancers and nodules may cause symptoms. In these cases, patients may complain of pain in the neck, jaw, or ear. If a nodule is large enough to compress the windpipe or esophagus, it may cause difficulty with breathing, swallowing, or cause a "tickle in the throat". Even less commonly, hoarseness can be caused if a thyroid cancer invades the nerve that controls the vocal cords.

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The important points to remember are that cancers arising in thyroid nodules generally do not cause symptoms, thyroid function tests are typically normal even when cancer is present, and the best way to find a thyroid nodule is to make sure that your doctor examines your neck as part of your periodic check-up.

WHAT CAUSES THYROID CANCER?

Thyroid cancer is more common in people who have a history of exposure to high doses of radiation, have a family history of thyroid cancer, and are older than 40 years of age. However, for most patients, we do not know the specific reason or reasons why thyroid cancer develops.

High dose radiation exposure, especially during childhood, increases the risk of developing thyroid cancer. Prior to the 1960s, X-ray treatments were often used for conditions such as acne, inflamed tonsils and adenoids, enlarged lymph nodes, or to treat enlargement of a gland in the chest called the thymus. All these treatments were later found to be associated with an increased risk of developing thyroid cancer later in life. Even X-ray therapy used to treat cancers such as Hodgkin's disease (cancer of the lymph nodes) or breast cancer has been associated with an increased risk for developing thyroid cancer if the treatment included exposure to the head, neck or chest. Routine X-ray exposure such as dental X-rays, chest X-rays and mammograms have not been shown to cause thyroid cancer.

Exposure to radioactivity released during nuclear disasters (1986 accident at the Chernobyl power plant in Russia or the 2011 nuclear disaster in Fukushima, Japan) has also been associated with an increased risk of developing thyroid cancer, particularly in exposed children, and thyroid cancers can be seen in exposed individuals as many as 40 years after exposure.

You can be protected from developing thyroid cancer in the event of a nuclear disaster by taking potassium iodide (see *Nuclear Radiation and the Thyroid brochure*). This prevents the absorption of radioactive iodine and has been shown to reduce the risk of thyroid cancer. The American Thyroid Association recommends that anyone living within 200 miles of a nuclear accident be given potassium iodide to take prophylactically in the event

of a nuclear accident. If you live near a nuclear reactor and want more information about the role of potassium iodide, check the recommendations from your state at the following link: www.thyroid.org/web-links-for-important-documents-about-potassium-iodide/.

HOW IS THYROID CANCER DIAGNOSED?

A diagnosis of thyroid cancer can be suggested by the results of a fine needle aspiration biopsy of a thyroid nodule and can be definitively determined after a nodule is surgically excised (see *Thyroid Nodule brochure*). Although thyroid nodules are very common, less than 1 in 10 will be a thyroid cancer.

WHAT IS THE TREATMENT FOR THYROID CANCER?

Surgery. The primary therapy for all types of thyroid cancer is surgery (see Thyroid Surgery brochure). The extent of surgery for differentiated thyroid cancers (removing only the lobe involved with the cancer-called a lobectomyor the entire thyroid – called a total thyroidectomy) will depend on the size of the tumor and on whether or not the tumor is confined to the thyroid. Sometimes findings either before surgery or at the time of surgery – such as spread of the tumor into surrounding areas or the presence of obviously involved lymph nodes - will indicate that a total thyroidectomy is a better option. Some patients will have thyroid cancer present in the lymph nodes of the neck (lymph node metastases). These lymph nodes can be removed at the time of the initial thyroid surgery or sometimes, as a later procedure if lymph node metastases become evident later on. For very small cancers (<1 cm) that are confined to the thyroid, involving only one lobe and without evidence of lymph node involvement a simple lobectomy (removal of only the involved lobe) is considered sufficient. Recent studies even suggest that small tumors - called micro papillary thyroid cancers may be observed without surgery depending on their location in the thyroid. After surgery, most patients need to

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be on thyroid hormone for the rest of their life (see *Thyroid Hormone Treatment brochure*). Often, thyroid cancer is cured by surgery alone, especially if the cancer is small. If the cancer is larger, if it has spread to lymph nodes or if your doctor feels that you are at high risk for recurrent cancer, radioactive iodine may be used after the thyroid gland is removed.

Radioactive iodine therapy. (Also referred to as I-131 therapy). Thyroid cells and most differentiated thyroid cancers absorb and concentrate iodine. That is why radioactive iodine can be used to eliminate all remaining normal thyroid tissue and potentially destroy residual cancerous thyroid tissue after thyroidectomy (see Radioactive Iodine brochure). The procedure to eliminate residual thyroid tissue is called radioactive iodine ablation. This produces high concentrations of radioactive iodine in thyroid tissues, eventually causing the cells to die. Since most other tissues in the body do not efficiently absorb or concentrate iodine, radioactive iodine used during the ablation procedure usually has little or no effect on tissues outside of the thyroid. However, in some patients who receive larger doses of radioactive iodine for treatment of thyroid cancer metastases, radioactive iodine can affect the glands that produce saliva and result in dry mouth complications. If higher doses of radioactive iodine are necessary, there may also be a small risk of developing other cancers later in life. This risk is very small, and increases as the dose of radioactive iodine increases. The potential risks of treatment can be minimized by using the smallest dose possible. Balancing potential risks against the benefits of radioactive iodine therapy is an important discussion that you should have with your doctor if radioactive iodine therapy is recommended.

If your doctor recommends radioactive iodine therapy, your TSH will need to be elevated prior to the treatment. This can be done in one of two ways.

The first is by stopping thyroid hormone pills (levothyroxine) for 3-6 weeks. This causes high levels of TSH to be produced by your body naturally. This results in hypothyroidism, which may involve symptoms such as fatigue, cold intolerance and others, that can be significant. To minimize the symptoms of hypothyroidism

your doctor may prescribe T3 (Cytomel[®], liothyronine) which is a short acting form of thyroid hormone that is usually taken after the levothyroxine is stopped until the final 2 weeks before the radioactive iodine treatment.

Alternatively, TSH can be increased sufficiently without stopping thyroid hormone medication by injecting TSH into your body. Recombinant human TSH (rhTSH, Thyrogen®) can be given as two injections in the days prior to radioactive iodine treatment. The benefit of this approach is that you can stay on thyroid hormone and avoid possible symptoms related to hypothyroidism.

Regardless of whether you go hypothyroid (stop thyroid hormone) or use recombinant TSH therapy, you may also be asked to go on a low iodine diet for 1 to 2 weeks prior to treatment (see *Low Iodine Diet FAQ*), which will result in improved absorption of radioactive iodine, maximizing the treatment effect.

TREATMENT OF ADVANCED THYROID CANCER.

Thyroid cancer that spreads (metastasizes) outside the neck area is rare, but can be a serious problem. Surgery and radioactive iodine remain the best way to treat such cancers as long as these treatments continue to work. However, for more advanced cancers, or when radioactive iodine therapy is no longer effective, other forms of treatment are needed. External beam radiation directs precisely focused X-rays to areas that need to be treated—often tumor that has recurred locally or spread to bones or other organs. This can kill or slow the growth of those tumors. Cancer that has spread more widely requires additional treatment.

New chemotherapy agents that have shown promise treating other advanced cancers are becoming more widely available for treatment of thyroid cancer. These drugs rarely cure advanced cancers that have spread widely throughout the body but they can slow down or partially reverse the growth of the cancer. These treatments are usually given by an oncologist (cancer specialist) and often require care at a regional or university medical center.

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WHAT IS THE FOLLOW-UP FOR PATIENTS WITH THYROID CANCER?

Periodic follow-up examinations are essential for all patients with thyroid cancer because the thyroid cancer can return—sometimes several years after successful initial treatment. These follow-up visits include a careful history and physical examination, with particular attention to the neck area. Neck ultrasound is an important tool to view the neck and look for nodules, lumps or cancerous lymph nodes that might indicate the cancer has returned. Blood tests are also important for thyroid cancer patients. Most patients who have had a thyroidectomy for cancer require thyroid hormone replacement with levothyroxine once the thyroid is removed (see *Thyroid Hormone Treatment* brochure). The dose of levothyroxine prescribed by your doctor will in part be determined by the initial extent of your thyroid cancer. More advanced cancers usually require higher doses of levothyroxine to suppress TSH (lower the TSH below the low end of the normal range). In cases of minimal or very low risk cancers, it's typically safe to keep TSH in the normal range. The TSH level is a good indicator of whether the levothyroxine dose is correctly adjusted and should be followed periodically by your doctor.

Another important blood test is measurement of thyroglobulin (Tg). Thyroglobulin is a protein produced by normal thyroid tissue and thyroid cancer cells, and is usually checked at least once a year. Following thyroidectomy and radioactive iodine ablation, thyroglobulin levels usually become very low or undetectable when all tumor cells are gone. Therefore, a rising thyroglobulin level should raise concern for possible cancer recurrence. Some patients will have thyroglobulin antibodies (TgAb) which can make it difficult to rely on the Tg result, as this may be inaccurate.

In addition to routine blood tests, your doctor may want to repeat a whole-body iodine scan to determine if any thyroid cells remain. Increasingly, these scans are only done for high risk patients and have been largely replaced by routine neck ultrasound and thyroglobulin measurements that are more accurate to detect cancer recurrence, especially when done together.

WHAT IS THE PROGNOSIS OF THYROID CANCER?

Overall, the prognosis of differentiated thyroid cancer is excellent, especially for patients younger than 45 years of age and those with small cancers. Patients with papillary thyroid cancer who have a primary tumor that is limited to the thyroid gland have an excellent outlook. Ten year survival for such patients is 100% and death from thyroid cancer anytime thereafter is extremely rare. For patients older than 45 years of age, or those with larger or more aggressive tumors, the prognosis remains very good, but the risk of cancer recurrence is higher. The prognosis may not be guite as good in patients whose cancer is more advanced and cannot be completely removed with surgery or destroyed with radioactive iodine treatment. Nonetheless, these patients often are able to live a long time and feel well, despite the fact that they continue to live with cancer. It is important to talk to your doctor about your individual profile of cancer and expected prognosis. It will be necessary to have lifelong monitoring, even after successful treatment.





